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# Desmoplastic Small Round Cell Tumor of Pancreatic Origin in a Young Child: A Case Report and Review of Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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**Conflict of interest:** None declared

**Patient:** Male, 9-year-old
**Final Diagnosis:** Desmoplastic small round cell tumor • pancreatic cancer
**Symptoms:** Abdominal pain
**Medication:** —
**Clinical Procedure:** —
**Specialty:** Pathology

**Objective:** Rare disease

**Background:** Desmoplastic small round cell tumor (DSRCT) is a rare lethal malignant tumor with young male predominance. The majority of cases arise in the abdominopelvic region and are hypothesized to have a mesothelial origin. However, extra-abdominal and extraperitoneal DSRCT have been reported. It is extremely uncommon for the pancreas to be a primary site for DSRCT, and only 5 cases have previously been reported in the English literature. Clinically, DSRCT has a wide range of presentations from asymptomatic to life-threatening comorbidity, and it responds poorly to treatment despite aggressive therapy.

**Case Report:** We report a previously healthy 9-year-old boy with an incidentally discovered abdominal mass of pancreatic origin. All necessary laboratory investigations were within normal limits. Computed tomographic imaging showed a huge left-side retroperitoneal mass measuring 15 cm in the greatest dimension that was accompanied by vascular encasement. The mass was resected successfully. Histopathological examination along with ancillary tests favored a diagnosis of DSRCT over other small round blue cell tumors. Detection of translocation t(11;22)(p13;q12) with *EWSR1-WT1* gene fusion, based on reverse transcription-polymerase chain reaction analysis, confirmed the diagnosis. Approximately 7 months later, the tumor recurred with mesenteric lymph nodes metastasis and the child was placed on palliative therapy.

**Conclusions:** It is worthwhile to consider DSRCT in the differential diagnosis of small round blue cell tumors, even in unusual sites, in a pediatric age group. Due to the poor prognosis, owing to chemotherapy resistance and a high rate of recurrence with significant tumor burden, reaching a precise diagnosis of DSRCT is essential. Almost all cases harbor the hallmark molecular alteration of t(11;22)(p13;q12) with *EWSR1-WT1* gene fusion. Debulking surgery paired with a chemotherapy regimen comprising vincristine, doxorubicin, and cyclophosphamide and ifosfamide+etoposide has been shown to improve overall survival rate compared with other chemotherapeutic agents. However, no targeted therapeutic modality has been developed.

**MeSH Keywords:** Desmoplastic Small Round Cell Tumor • Pancrelipase • Pediatrics

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## Background

In 1989, desmoplastic small round cell tumor (DSRCT) was recognized as a separate entity by Gerald and Rosai [1]. This rare malignant tumor predominantly affects children and adolescent males, with a peak incidence in the third decade of life [2]. Usually, it arises from serosal surfaces, mainly the peritoneum. The second most common site is the abdominopelvic region, with no distinct organ involvement. However, DSRCT arising from various body organs, such as pleura, ovary, testis, central nervous system, orbit, and others, has been described [3,4]. Primary pancreatic DSRCT is extremely rare, limited only to 5 reported cases in the available English literature (Table 1). Since DSRCT has nonspecific imaging features, microscopic examination is very helpful because it shows malignant cells with primitive morphology of undifferentiated round blue cells separated by the cellular desmoplastic stromal reaction. In addition, immunohistochemistry expression of mixed mesenchymal, epithelial, and neural markers is exclusively supportive. The most accurate, well-established molecular analysis is by reverse transcription-polymerase chain reaction (RT-PCR) or fluorescence *in situ* hybridization (FISH), which identify translocation t(11;22)(p13;q12) with *EWSR1-WT1* gene fusion. A modality of combined surgery, chemotherapy, and radiotherapy is the mainstay of management. In general, DSRCT behaves aggressively and is associated with very poor prognosis. Hence, proper identification of DSRCT is of great value. Herein, we describe a rare case of DSRCT originating from the pancreas in an asymptomatic child.

## Case Report

A previously healthy 9-year-old boy presented to a pediatric surgery clinic with a history of abdominal mass accompanied by intermittent abdominal pain during the 3 months before admission. The mass was incidentally discovered at an outside facility after the boy experienced a mild abdominal trauma. Physical examination demonstrated firmness on the left side of the abdomen. Otherwise, the child was alert and in good general condition. Laboratory investigations, including blood profile, renal and liver function tests, coagulation profile, electrolytes, and urine analysis, were within normal limits. Amylase was 165 U/L and lipase was 259 U/L; tumor markers were not performed. Abdominal computed tomography (CT) scan with contrast showed a left flank soft tissue abdominal mass (15×10.1×6.5 cm) that extended from the splenic hilum down to the level of the aorta bifurcation. The mass was associated with significant vascular encasement, and it was not separable from the pancreatic body and tail. No definite hepatic or splenic lesions were present (Figure 1A). Radiological impression included neuroblastoma, lymphoma, and neuroendocrine tumor. The patient underwent exploratory laparotomy for debulking and removal of the tumor with distal pancreatectomy, splenectomy, splenic flexure, and colon segment resection. Microscopic examination depicted an infiltrative neoplastic growth arranged in well-defined, relatively sharply demarcated nests embedded in the dense desmoplastic stroma. The neoplastic cells exhibited features of small round blue cells with increased nuclear to stromal ratio, hyperchromatic nuclei, and scarce cytoplasm (Figure 1B, 1C). To reach a specific diagnostic entity, a panel of immunohistochemistry markers were assayed. Neoplastic cells were immunoreactive to vimentin, desmin (Figure 1D), CD56 (Figure 1E), CD57, and neuron-specific enolase (Figure 1F). They showed focal positivity for EMA, SMA, CD15, and CD99. A few cells showed weak staining for CK8/18. Assays were negative for pan-cytokeratin, MSA, myogenin, Myo-D1, chromogranin, synaptophysin, CD34, CD31, CD117, and CA19-9. Tumor staining for WT-1 was inconclusive. The aforementioned tumor morphology along with the immunophenotype raised our suspicion for DSRCT. A molecular study for t(11;22) *EWSR1-WT1* gene fusion using RT-PCR was conducted at the Mayo Clinic. The result confirmed our diagnosis of DSRCT arising from the pancreas. There is no specific tumor marker for DSRCT. The patient completed 6 cycles of chemotherapy using the non-rhabdomyosarcoma protocol including ifosfamide, doxorubicin, and vincristine with a 3-week interval between each cycle for 15 weeks. Seven months later, the patient appeared severely ill with marked deterioration, and a recurrence of the mass was suspected. Imaging was not available, and he underwent another exploratory laparotomy for resection of the recurred mass and dissection of mesenteric lymph nodes. Histopathological examination showed morphology identical to the initial DSRCT consistent with recurrence and metastasis. The patient was placed on palliative treatment to improve his quality of life and to increase the symptom-free survival time through disease stabilization. He was also provided with psychological and social support.

## Discussion

DSRCT is an uncommon sarcomatous neoplasm with a young male predilection. Most of the reported cases were found to arise in the pelvic and intra-abdominal region [5]. Although the most common site is the peritoneum, extraperitoneal DSRCT has been described in various body organs, such as the parotid gland, ovary, testis, and pleura, and orbit [2–4]. To the best of our knowledge, only 5 reported cases have described DSRCT in the pancreas as a predominant intra-abdominal solid organ involvement [6–10] (Table 1). Individuals with DSRCT present with various clinical presentations, from asymptomatic to a complex large intra-abdominal mass manifested as abdominal pain or symptoms of compression. Only one previously reported case included painful obstructive jaundice [8]. Our case is interesting as the mass was discovered incidentally after mild





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**Table 1.** Summary of reported cases of primary pancreatic desmoplastic small round cell tumor including the present case.

| Pt. No. | Author [reference] | Age/sex | Presentation | Duration of symptoms/ complaint | Metastasis | Therapy | Outcome |
|---|---|---|---|---|---|---|---|
| 1 | Present case | 9 years/ Male | Abdominal pain | 3 months | Mesenteric lymph nodes | Distal pancreatectomy, splenectomy, splenic flexure, and colon segment resection+six cycles of non-RMS chemotherapy | Recurrence at 7 months |
| 2 | Bismar TA et al. 2004 [6] | 31 year/ Female | Enlarging abdomen | 2 months | Smaller nodules on the peritoneal surfaces, bilaterally on ovarian surfaces and pelvis | Subtotal pancreatectomy with partial stomach resection | NA* |
| 3 | Seshadri A et al. 2014 [7] | 40 year/ Female | Abdominal pain | 2 years | peritoneal deposits confined to lesser omentum and anterior surface of transverse mesocolon | Distal pancreatectomy, splenectomy, and left upper quadrant peritonectomy+three cycles of chemotherapy (MESNA, etoposide based) | No recurrence at 6 months |
| 4 | Subasinghe D et al. 2014 [8] | 24 year/ Male | Rapidly progressive obstructive jaundice associated with abdominal pain | 1 month | No evidence of peritoneal or liver metastases | Whipple's procedure+adjuvant combination chemotherapy (vincristine, cyclophosphamide, doxorubicin, ifosfamide and etoposide) | No recurrence at 6 months |
| 5 | Qureshi SS et al. 2011 [9] | 16 year/ Female | Abdominal lump | 1 month | Negative | Chemotherapy (9 weeks), then distal pancreatectomy with splenectomy, transverse colon resection was performed | No recurrence at 14 months |
| 6 | Albiruni R et al. 2007 [10] | 35 year/ Female | Progressive abdominal pain and weight loss | 5 months | At least two large liver metastases | Vinorelbine/ cyclophosphamide | NA* |

* NA – not available.

abdominal trauma. It subsequently progressed rapidly, and it was found to arise from the pancreas. It adhered to the spleen, splenic flexure, and part of the colon, which required aggressive surgical removal through exploratory laparotomy. In this case, the pancreas was almost replaced by the tumor. The distal part was involved initially, followed by involvement of the head of the pancreas. However, there was no evidence of pelvic, omental, or peritoneal deposits or ascites, which made a primary peritoneal DSRCT with invasion to the pancreas less likely. Histopathologic features of this tumor helped to reach the diagnosis. The malignant cells exhibited features of primitive cells with scant cytoplasm and hyperchromatic nuclei with inconspicuous nucleoli. They were arranged in variable histologic patterns and formed tubules or nests encircled by dense desmoplastic fibro-myxoid stroma. The diagnosis of this tumor is challenging in children, even with known polyphenotypic immunohistochemistry markers, because it does not have a specific radiological image and it may show various types of differentiation such as epithelial, mesenchymal, or neuronal [11]. Characteristically, DSRCT expresses desmin in a dot-like pattern, as in our case, and nuclear positivity for WT-1 along with immunoreactivity for an epithelial component favors DSRCT over other small round blue cell tumors. Unfortunately, WT-1 was inconclusive in our case. However, the current case was negative for myogenin and MyoD1, which made rhabdomyosarcoma unlikely. In addition, the negativity for chromogranin





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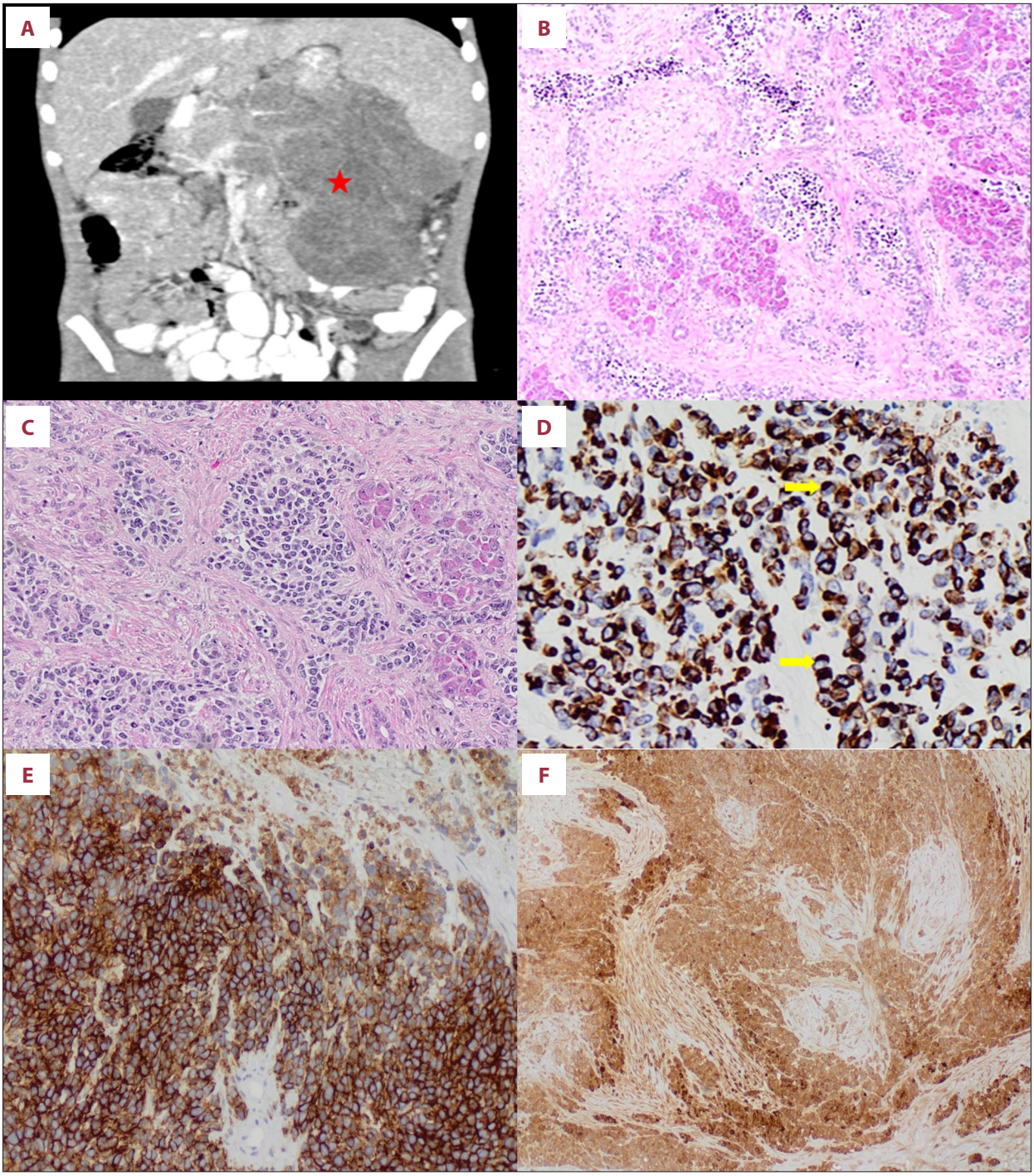


**Figure 1.** Radiology and histopathology (hematoxylin and eosin stain [H&E]) examination of the mass. (**A**) Abdominal computed tomography (CT) scan with contrast. The axial view depicts a large left flank abdominal tumor (15×10.1×6.5 cm; red star) with extensive retroperitoneal and midline extension with distorted pancreatic tissue and significant vascular encasement. (**B**) (×4; H&E) Sharp demarcated nests formed of undifferentiated small round blue cells surrounded by dense desmoplastic stromal reaction are embedded within the pancreatic parenchyma. (**C**) (×10; H&E) Nuclear features of DSRCT are primitive-appearing uniform nuclei that exhibit increased nuclear to stromal ratio, dense chromatin, inconspicuous nucleoli, and scant to clear cytoplasm. (**D**) (×10) The majority of the tumor cells are expressing desmin in a characteristic perinuclear dot-like pattern (yellow arrows). (**E**) (×10) DSRCT displays strong membranous expression for CD56. (**F**) (×4) Immunohistochemical staining of DSRCT for neuron-specific enolase indicates that most of the tumor cells were positive for this marker in the cytoplasmic staining pattern.





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and synaptophysin helped to rule out the possibility of neuroendocrine tumors. At the time, Ewing sarcoma/PNET could not be completely excluded due to focal membranous positivity for a highly sensitive marker, CD99. However, CD99 is not specific, and many other small round blue cell tumors may express it. The diagnosis of DSRCT was confirmed by detecting a characteristic cytogenetic abnormality of gene fusion between the *EWSR1* gene on chromosome 22 and the *WT1* gene on chromosome 11, which is expressed as t(11;22)(p13;q12), using RT-PCR. Conversely, Ewing sarcoma/PNET has a unique reciprocal translocation t(11;22)(q24; q12) between the *EWSR1* and *FLI1* genes. DSRCT possesses aggressive behavior and poor prognosis, with a median survival rate of 17 months (range 3–72) [8]. Hence, its recognition is of extreme importance. The tumor in our patient recurred with metastasis to mesenteric lymph nodes 7 months after removal of the initial mass and 6 cycles of chemotherapy of non-rhabdomyosarcoma protocol. There are no known differences between the typical versus pancreatic DSRCT. To date, there is no targeted therapy for DSRCT, but a combination of surgical debulking; chemotherapy using a high-dose P6 regimen including doxorubicin, cyclophosphamide, and vincristine; and radiotherapy results in a better impact on the stability of the disease. Alternatively, ifosfamide and etoposide regimen may be used [12]. The 3- and 5- year survival rates in patients with DSRCT have been documented to be 44% and 15%, respectively [12].

## Conclusions

Despite the rarity cases of DSRCT, even in the classic abdominopelvic cavity, several studies have documented DSRCT arising in a different body organs including the pancreas. Considering DSRCT within the continuum of differential diagnoses of small round blue cell tumors, particularly in extraperitoneal locations, is beneficial. However, there are no known significant differences between pancreatic compared with primary peritoneal DSRCT. Reaching a precise diagnosis of DSRCT is essential because the behavior and management of this neoplasm may differ markedly. In challenging cases, the characteristic translocation and fusion gene (*EWSR1-WT1*) can be exploited for diagnosis even in unusual sites.

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