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CASE REPORT

Desmoplastic Small Round Cell Tumor: A Rare Case of Extraluminal Bowel Obstruction and Review of the Literature

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Introduction

Desmoplastic small round cell tumor (DSRCT) is an extremely rare malignant neoplasm that was first described by Sesterhenn et al. [1]. Its estimated incidence is between 0.2 and 0.5 per million per year [2]. DSRCT has been characterized as a highly aggressive cancer, which predominantly affects male adolescents and young adults. It usually presents as multiple widespread peritoneal and omental implants within the abdomen and pelvis [3]. Peritoneal metastasis is almost always present at diagnosis, and concurrent extraperitoneal metastases have been found in 47% of patients [4]. Four good prognostic factors include absence of extraperitoneal metastasis, macroscopic resection of peritoneal disease, whole abdominopelvic radiotherapy, and postoperative chemotherapy. Herein, we describe a 25-year-old male patient who presented with constipation and abdominal distension and subsequently diagnosed with desmoplastic small round cell tumor.

Case

A 25-year-old male with no known past medical history was admitted for constipation, bloating, right upper quadrant abdominal pain, and worsening abdominal distension. He reported an associated 20 lbs, unintentional weight loss, and decreasing appetite over the prior 2 months. He admitted to occasional alcohol consumption and cigarette smoking. The patient denied a family history of cancer. Physical examination was significant for a hard mass palpated in the left upper quadrant and distension of the abdomen. Heart rate was 97.6/min, blood pressure was 136/90 mmHg, respiratory rate was 20/min, oxygen saturation was 97% on room air, and temperature was 97.6 °F. Laboratory results were within normal limits with a white blood cell (WBC) count of 9.5/ul, hemoglobin of 13.3 g/dl, and hematocrit of 41%, but platelet count of 586 k/cmm.

Computed tomography (CT) scan of the abdomen and pelvis revealed a moderate amount of ascites particularly in the perihepatic and perisplenic region and also within the right lower quadrant and small bowel mesentery. Innumerable individual and conglomerate masses were identified throughout the abdomen and pelvis, the largest of which was heterogeneous with areas of low density consistent with necrosis. Multiple peritoneal or omental implants were also noted along with evidence of bowel obstruction at the level of the sigmoid colon (Fig. 1).

Needle biopsy of the abdominal mass revealed malignant epithelioid neoplasm composed of sheets and nests of small cells and slightly larger, clear cells, embedded in abundant fibrotic and desmoplastic stroma. The nuclei were round to oval and hyperchromatic with small inconspicuous nucleoli. Immunohistochemical stains showed expression of cytokeratin (CAM5.2 and AE1/AE3), desmin, CD99, and FLI1 and negative for WT1, S100, synaptophysin, and chromogranin (Fig. 2). Fluorescence in situ hybridization (FISH) assay for EWSR1-WT1 rearrangement was positive, consistent with DSRCT. The FISH analysis was conducted using a fusion probe, and the immunohistochemical staining for WT1 was carried out using clone WT49 (Leica Biosystems) against the N-terminus. Clone dilution was not required according to manufacturer's instructions.

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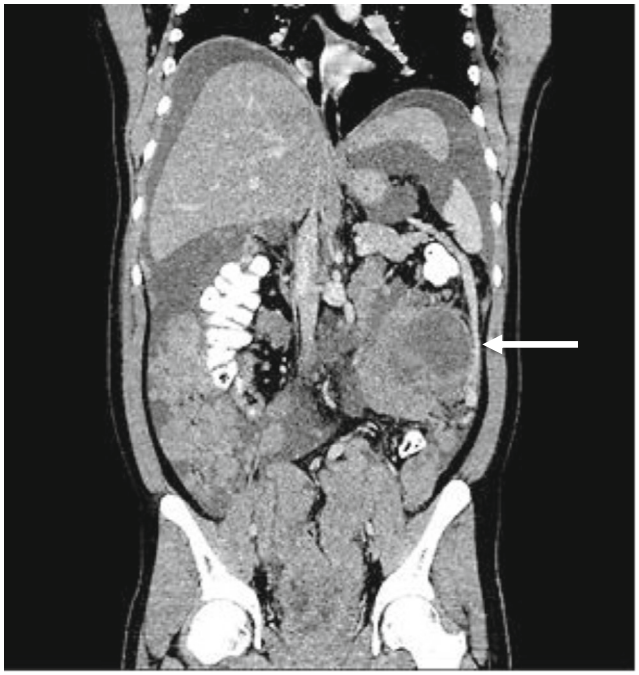

Fig. 1 Sigmoid colon compression by extra luminal mass (arrow)

Discussion

Desmoplastic small round cell tumor is an extremely rare tumor. Sesterhenn et al. (1987) described 17 young males with DSRCT arising in the pelvis or scrotum [5, 6]. While research into this disease has helped to understand its nature and progression, DSRCT still remains a challenge to diagnose and manage for clinicians. An estimated 96% of patients with DSRCT are males in their second or third decade of life, without ethnic predilection [7]. Owing to its aggressive behavior, only 29% of patients survive past 3 years [6].

This malignancy usually appears with extensive peritoneal and omental implants within the abdomen and pelvis, without any apparent organ of origin. Despite its remarkable size, there are no early warning signs as majority of patients are young and healthy. The tumor is uninhibited and spreads throughout the abdomen and pelvis before symptoms present. However, at the time of presentation, the most common signs are abdominal pain, distension, decreased appetite, and palpable abdominal mass [8]. Our patient presented with similar symptoms in addition to constipation caused by extra luminal compression of his sigmoid colon.

DSRCT shares morphological similarities with other small round cell tumors such as Ewing's sarcoma, small cell mesothelioma, neuroblastoma, lymphoma, primitive neuroectodermal tumor, rhabdomyosarcoma, and Wilm's tumor [8]. The diagnosis requires immunohistochemistry to aid in differentiating DSRCT from other similar neoplasms. Typically, biopsy followed by histopathology reveals clusters of small to medium sized cells with hyperchromatic nuclei and increased nuclear to cytoplasm ratio, surrounded by a dense desmoplastic stroma [5]. Immunohistochemistry may also demonstrate a trilinear co-expression of keratin, desmin, and vimentin [9–12].

The formal diagnosis of DSRCT is based on a unique reciprocal translocation, t(11;22)(p13;q12), which was identified in 1992 [13]. A defining feature, the translocation fuses the EWSR1 gene on chromosome 22 to the WT1 gene on chromosome 11 [12]. The fused transcript encodes the N-terminus of EWSR1 and the C-terminus (DNA-binding domain) of WT1 [14]. In the majority of cases, the resultant chimera contains the first seven exons of EWSR1 and the last

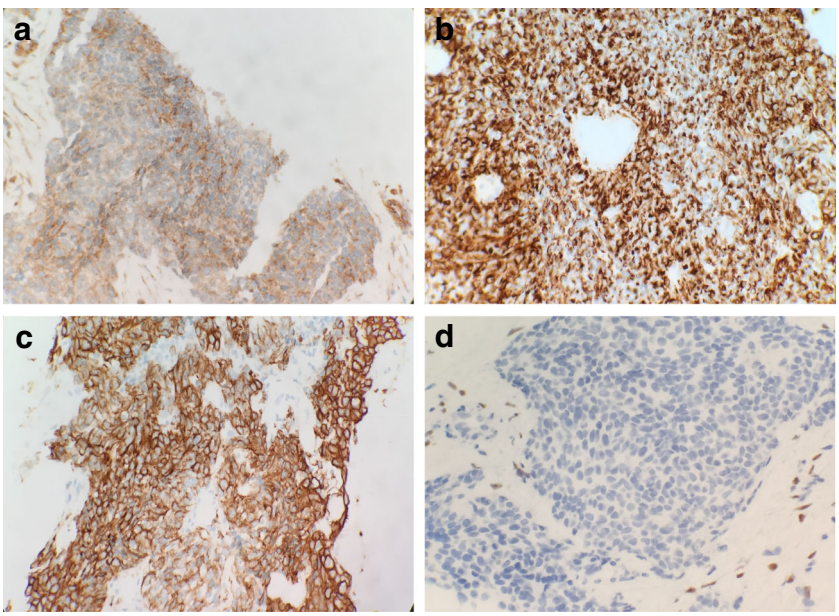

Fig. 2 **a** Tumor cells are immunopositive for AE1/AE3 (× 40). **b** Immunopositive for desmin (× 40). **c** Immunopositive for CD99 (× 40). **d** Immunonegative for N-terminal WT1 (× 40)

three exons (exons 8–10) of the WT1 gene [14]. However, several variants have been described with alternative breakpoints for the t(11;22)(p13;q12) translocation containing additional exons from EWSR1 with WT1 conservation.

Immunohistochemical staining for WT1 is usually positive in 90% of cases and can be useful in the diagnosis of DSRCT [15]. Several studies recognize that WT1 expression in DSRCT may be a diagnostic marker of this tumor [10, 11, 16]. Barnoud et al. (2000) reported that WT1 immunoreactivity was not observed in Ewing's sarcoma/primitive neuroectodermal tumors, neuroblastomas, or rhabdoid tumors of the kidney, while nephroblastomas and rhabdomyosarcomas showed focal nuclear staining [10]. The latter two were reconciled with clinical correlation of tumor characteristics.

However, variation in WT1 expression may be misleading without polymerase chain reaction (PCR) for the EWSR1-WTI transcript, which is more specific in confirming DSRCT [17]. Alternatively, weak or absent WT1 expression in the presence of EWSR1-WT1 fusion transcript has been reported as a rare molecular variant of DSRCT, thus, necessitating further testing for EWSR1-WT1. For this paper, we did not pursue gene sequencing to identify the molecular characteristics of the translocation. However, according to literature, the incidence of WT1 negative DSRCT ranges from approximately 11 to 30% [18–20]. Typically, WT1 demonstrates C-terminus antibody reactivity without N-terminus antibody reactivity. In rare instances, DSRCT can present with WT1 N-terminus reactivity while negative for the WT1 C-terminal. Murphy et al. (2008) reported a rare EWS-WT1 fusion transcript that was confirmed by PCR. Immunostaining was positive at the N-terminus and negative at the C-terminus and strongly expressed full-length WT1 [15].

Lae et al. (2002) reviewed 32 cases of DSRCT and reported 91% (29 of 32) positive WT1 staining [21]. The three cases which exhibited no immunoreactivity for WT1 also showed no reactivity for desmin. However, variable expression of desmin was not correlated with WT1 reactivity. Zhang et al. (2003), while emphasized the use of a panel of multiple myoid and epithelial markers for the workup of DSRCT, reported that desmin and CAM5.2 (both 91%) were the most sensitive diagnostic markers, both of which were found positive in our case [19].

Owing to its aggressive behavior, the exact therapeutic approach is unclear. In patients without extraperitoneal metastasis, a multimodal treatment combining systemic chemotherapy, complete macroscopic resection, and postoperative whole abdominopelvic radiotherapy could enable prolonged survival [4]. However, given its nature, regardless of a combined therapeutic strategy of surgical intervention and radiotherapy, patient prognosis remains very poor, approximately 29% for a 3-year survival and just 18% for a 5-year survival [22, 23].

Conclusion

We report a rare case of DSRCT which was confirmed with FISH analysis. The extent of tumor invasion in our patient's abdomen led to extra luminal bowel obstruction. Its pathogenesis stems from a chromosomal translocation where the resultant chimeric transcript fails functional tumor suppression capacity. Clinicians should have knowledge of interpreting WT1 staining and antibody target epitopes in order to facilitate accurate diagnosis of DSRCT. Since the number of variants reported is low, information on prognosis and therapeutic response remains limited. Overall, DSRCT is a highly aggressive neoplasm with poor prognosis.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Consent Obtained.

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