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CASE REPORT

Desmoplastic Small Round Cell Tumor: A Rare but Aggressive Tumor in Young Women

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ABSTRACT

Desmoplastic small round cell tumor (DSRCT) is a rare malignant neoplasm. It is primarily found in young men, with a reported male to female ratio of 4:1. The tumor typically develops in the abdominal cavity, invading the omentum with multiple peritoneal implants involving the diaphragm, splenic hilum, mesentery of the small and large bowel, and the pelvic peritoneum. Most of them have widespread disease at presentation, with an organ of origin difficult to ascertain. We report a case of desmoplastic round cell tumor in a 17-year-old teenage girl. Immunohistochemistry helped in the diagnosis. She received multimodality treatment.

Keywords: Abdominal distension, Desmoplastic small round cell tumor, Immunohistochemistry, Multimodality treatment.

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INTRODUCTION

Desmoplastic small round cell tumor (DSRCT) is a rare malignant neoplasm.[1] Common presenting symptoms include abdominal pain and distension.[5] Unfortunately, DSRCT is often widely disseminated throughout the peritoneal cavity at diagnosis and quickly recurs despite treatment, so the prognosis is exceedingly poor.[5] DSRCT is associated with a unique chromosomal translocation t(11:22) (p 13; q 12) that involves the EWSR1 and WT1 genes.[3] In females, it is usually mistaken for ovarian tumor.

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CASE REPORT

Ms. P, a 17-year-old, presented to us with abdominal pain of 20 days duration. There were no aggravating or relieving factors. There were no other associated symptoms. Her menstrual cycles were regular with 5/30 days, but was associated with spasmodic dysmenorrhea. She gave a history of laparotomy 1 year prior for an ovarian cyst. The cyst had ruptured during the procedure and around 1,000 mL of hemorrhagic fluid was drained. The fluid was neither sent for cytology nor the cyst wall for histopathology.

On examination, she was moderately built and nourished. Her vital parameters were normal. Cardiovascular and respiratory systems were within normal limits. On per abdomen examination, a transverse suprapubic scar of 10 cm, healed by primary intention, was present. A vague mass was felt in left iliac fossa measuring 4×5 cm^2, which was firm and nontender. There was no free fluid. As she was not sexually active, per vaginal examination was deferred. Per rectal examination revealed uterus, which was bulky and a mass felt anterior measuring 8×7 cm^2. It was also nontender. Our provisional diagnosis was ovarian tumor/endometriosis.

Investigations

Complete blood count was within normal limits. Cancer antigen 125 was 9.8 IU/mL.

Ultrasonography

A large heterogeneous lesion at the lateral aspect of the uterus measured $8.5 \times 6.1 \times 6.8$ cm. A complex cystic lesion seen in the left iliac region measured $6.1 \times 6.9 \times 3.7$ cm with few thin and thick septations. Left ovary appeared to be abutting the lesion. Right side ovary measured 2×1.9 cm. A poorly defined heterogeneous lesion at splenic hilum measured 3 1.8 cm.

Computed Tomography Scan

A large heterogeneously enhancing mass measuring 7 cm in diameter with a craniocaudal extent of 7 cm involving the body was found on the right side of the uterus. The left ovary was bulky. Another lesion with solid and nonenhancing cystic component was observed deep to the anterior abdominal wall in the left lumbar region adherent

Fig. 1: Multiple deposits present all over the abdomen (*Source*: M.S. Ramaiah Medical Teaching Hospital, Bengaluru, Karnataka)

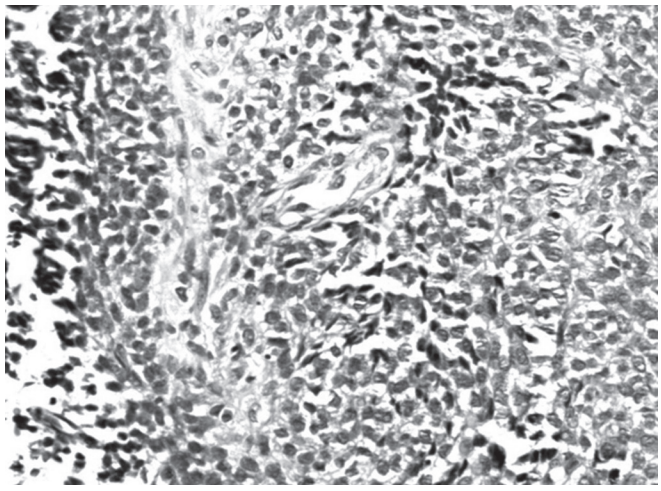

Fig. 2: Microscopy: Nests of small round blue tumor cells embedded in desmoplastic stroma. Small to medium size tumor cells with scanty cytoplasm (*Source*: M.S. Ramaiah Medical Teaching Hospital, Pathology Department, Bengaluru, Karnataka, India)

to parietal peritoneum, jejunum, and descending colon, measuring 4.5×7 cm^2 axially for a craniocaudal span of 8 cm, its inferior extremity abutting the left ovary. Another lesion at splenic hilum and an enlarged mesenteric lymph node in the left upper quadrant measured 12×20 mm.

Endoscopy and colonoscopy were normal. As no prior histopathology examination report was available and due to prior laparotomy, the decision was made for a repeat laparotomy and not laparoscopy (Fig. 1).

Exploratory laparotomy was done after arranging for frozen section. On opening the peritoneum, a cyst got ruptured and hemorrhagic fluid drained. Multiple jelly-like deposits were studded all over the abdomen. Uterus was bulky, and both ovaries appeared normal. There were no ascites. There were three masses adherent to omentum measuring 3×4 cm, 3×2 cm, and 3×5 cm. Para-aortic nodes were palpable.

Frozen Section

Hemorrhagic fluid – inflammatory response: The mass was found to be papillary carcinoma. There was a doubt whether primary tumor was from ovary or possibility of pancreas and hence Wedge biopsy the ovary was normal. As para-aortic nodes were enlarged, considering as stage IV, the abdomen was closed.

Histopathology examination report was as follows: Omental nodules – poorly differentiated carcinoma. If primary at known sites are ruled out, primary may be omentum/mesentery. Extragonadal germ cell tumor has to be ruled out.

Further investigations were planned. The other tumor markers carcinoembryonic antigen, cancer antigen 19.9, beta human chorionic gonadotropin, and alpha-fetoprotein were normal. Immunohistochemistry was positive for vimentin and synaptophysin. Leukocyte common antigen, chromogranin, epithelial membrane antigen, calretinin, and desmin were negative. This was consistent with desmoplastic round cell tumor. Repeat histopathologic examination helped in making the diagnosis of DSRCT (Fig. 2).

The patient received six cycles of chemotherapy with the following drugs: Cisplatin, doxorubicin, and cyclophosphamide. Due to financial constraint, carboplatin was not given. Three months later, repeat computed tomography (CT) scan showed solid and cystic heterogeneous mass of $4 \times 4.8 \times 5.2$ cm in the pelvis.

Repeat laparotomy was done. The abdomen appeared normal. There were no ascites. Uterus and ovaries were normal. No nodes were palpable. The mass was excised. Infracolic omentectomy was done.

Histopathology Examination Report

The mass was a mesenteric cyst. The omentum was free from metastasis.

She came for a regular follow-up. She was symptom-free for 2 years. Computed tomography scan was normal during this period. After 2 years, CT scan showed uterus enlarged in size measuring $12.8 \times 11 \times 9.5$ cm with a solid and cystic mass on the right side measuring 3.5×4.5 cm. It indicated recurrence of the tumor. We planned for hysterectomy with bilateral salpingo-oophorectomy and cytoreductive surgery, but due to social reasons, she refused hysterectomy. Laparotomy was done and mass was excised. It was a recurrence of the tumor.

After 8 months, she came with the inability to walk. Computed tomography scan showed a large heterogeneous mass in the midline in the infraumbilical region measuring $10 \times 13 \times 15$ cm. Aorta and inferior vena cava

were compressed by the mass. They caused compression of bilateral ureters with hydroureteronephrosis. Uterus and ovaries were not seen separately. Small subcentimeter-sized nodular opacities were seen in the posterior basal segment of the left lower lobe and anterior basal segment of right lower lobe. Small osteolytic lesions were seen in lumbar vertebrae.

Ultrasonography-guided fine needle aspiration of abdominal mass confirmed recurrence of tumor consistent with DSRCT.

Whole-body skeletal scan was done. There was involvement of ribs bilaterally, parietal bone, iliac bones, acetabulum, bodies of T4, L5, and S1 vertebrae. We planned for salvage chemotherapy, but patient succumbed to the disease within a week.

DISCUSSION

Desmoplastic small round cell tumor is a rare but aggressive malignancy with poor outcome.[6] Desmoplastic small round cell tumor is a rare clinical entity with only 12 prior reported cases in women in the English literature.[5] The tumor typically develops in the abdominal cavity, invading the omentum with multiple peritoneal implants involving the diaphragm, splenic hilum, mesentery of small and large bowel, and the pelvic peritoneum.[3]

Desmoplastic small round cell tumor mainly develops in adolescent and young adults, with a strong male predominance; the mean age at diagnosis is approximately 22 years and ranges from 6 to 49 years, the male to female ratio is 4:1.[7] It rarely occurs in females and when it occurs, it is often mistaken for ovarian malignancy. There are no risk factors, either familial or environmental. Typically, tumors consisting of immunohistochemical studies show polyphenotypic differentiation with expression of epithelial, neural, and muscle markers.[8] A recurrent specific chromosomal abnormality t(11:22) (p13:q12) has been reported in DSRCT. The breakpoints in this translocation involve two genes: EWS, which is altered in the t(11:22) (q24:q12) rearrangement characteristic of the Ewing's family of tumors, and WT1, which is a Wilms' tumor gene. EWS–WT1 chimeric transcripts are considered diagnostic of this disease.[8,9]

Symptoms

There are very few warning symptoms/signs. The patients are young and healthy. The tumor grows and spreads uninhibited within the abdominal cavity. Clinically, patients present symptoms of abdominal sarcomatosis, such as ascites, abdominal pain and/or distension, constipation or bowel obstruction, vomiting, and weight loss.[3]

Abdominal imaging by ultrasound, CT scan, or magnetic resonance imaging reveals multiple peritoneal masses (from millimeter-sized nodules to confluent sheets and dozens to hundreds of nodules up to 20 cm or greater). For complete staging, the search for visceral metastasis (hepatic and/or pulmonary) with CT scan is typically used.[3]

Pathology

Typically, tumors consist of small, undifferentiated cells, or spindle cells invested within an abundant desmoplastic stroma.[1] The tumor cells have hyperchromatic nuclei.

Immunohistochemical studies show polyphenotypic differentiation with expression of epithelial, neural, and muscle markers.[10]

Percutaneous open biopsy of the lesion should be evaluated by cytogenetics to confirm the characteristic translocation and WT1 fusion.[11]

Desmoplastic small round cell tumor is a member of the large family of small round cell tumors of childhood, together with primitive neuroectodermal tumor (Ewing sarcoma), alveolar and embryonal rhabdomyosarcoma, poorly differentiated synovial sarcoma, and rhabdoid tumors.[3]

Disease staging and stage classification are essential to patient management and allow the comparison of different therapeutic strategies.[3] Currently, there is no formal staging system for DSRCT. A staging system proposed is still awaiting validation.[11]

Treatment

Therapeutic management of DSRCT remains challenging with low efficacy despite the combination of aggressive treatments, such as polychemotherapy, debulking surgery, and whole-body radiation.[3]

Aggressive surgical debulking is the mainstay of therapeutic strategy.[3] There is no gold standard chemotherapy regimen, but there is evidence that a high-dose alkylator-based regimen improves survival.[5] The "P6 protocol involves 7 courses of chemotherapy, courses 1-3 and 6 use cyclophophamide, doxorubicin and vincristine. Courses 4, 5 and 7 are infusions of ifosfamide and etoposide.[6]

Several authors have advocated the use of hyperthermic intraperitoneal chemotherapy (HIPEC) following optimal debulking in patients with DSRCT.[3] In DSRCT, HIPEC has been given as heated cisplatin at a dose of 100 to 150 mg/m^2.

Whole abdominopelvic (WAP) radiotherapy has also been proposed as an adjunct to (complete) surgery with the aim to improve local control.[3]

More recently, Pinnix et al reported a series of eight patients treated with WAP intensity-modulated radiation therapy (IMRT) after neoadjuvant chemotherapy and

debulking surgery.[12] Recently, yttrium microspheres have been found to be successful in treating diffuse liver metastasis from DSRCT.[11]

Prognosis

Despite aggressive multimodal treatment, median survival ranges from 17 to 25 months,with fewer than 20% of patients achieving 5-year survival.[3]

CONCLUSION

Desmoplastic small round cell tumor is a rare abdominal tumor, which requires neoadjuvant and adjuvant chemotherapy as well as complete surgical excision.[11] The impact of new techniques, such as HIPEC or IMRT needs to be clearly defined, ideally in the context of prospective randomized clinical trials since retrospective data to date give no sense of a positive survival signal.[3] Yttrium microsphere is a novel treatment for liver metastasis in DSRCT.[11]

Whole-genome sequencing of DSRCT is ongoing to identify mutations, single nucleotide polymorphisms, or copy number changes associated with these tumors to explore pathogenesis and open medical therapeutic possibilities.[3]

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