Unusual morphology of desmoplastic small round cell tumor from an ascitic fluid in the postchemotherapy setting

ABSTRACT
Desmoplastic small round cell tumor (DSRCT) is a malignant neoplasm that most often presents in male adolescents as an abdominal mass. Cytological features have been previously described, but only two reports noted post chemotherapy changes on effusions. We report a case of a 15-year-old male with DSRCT status postchemotherapy that presented with ascitis. Unusual morphology was seen: Numerous malignant large and single cells with prominent nucleoli and abundant cytoplasm in a background without the stroma, occasional mitosis, and the abundant apoptosis. Cell block immunocytochemistry was confirmatory. Awareness of the postchemotherapy changes in this tumor will allow us to diagnose recurrence.

Key words: Cytology; desmoplastic small round cell tumor; effusion, post chemotherapy

Introduction
Desmoplastic small round cell tumor (DSRCT) is a malignant neoplasm that was first described in 1987 but was only clinically recognized in 1989.[1,2] It predominantly affects young males, and it typically presents as a large intraabdominal mass with smaller peritoneal implants.[3]

Histologically, it is formed by nests of small round cells within a desmoplastic stroma. Immunohistochemically, it shows a polyphenotypic differentiation with positivity for epithelial, mesenchymal, myogenic, and neural markers.[2]

Our aim is to describe the unusual findings of DSRCT on a postchemotherapy setting and to create awareness of such changes.

Case Report
The clinical history is that of a 13-year-old male who complained of dysuria and was found to have a 16 cm pelvic mass, adhered to the bladder and two liver nodules. Open biopsy showed a DSRCT with classic morphology and immunohistochemistry findings. He received 1-year of chemotherapy, which included: Ifosfamide, etoposide, vincristine, cyclophosphamide, doxorubicin, and vincristine). Six months after, the liver mass decreased in size and he was started on total abdominal radiotherapy (until complete 4500 cgys). He received a total of 11 cycles of chemotherapy and 44 cycles of radiotherapy and was found to have a good response to treatment with persistence of the pelvic mass. He was taken to surgery 14 months after primary diagnosis and was found to have irresectable mass that surrounded bladder and ureters. The pathology showed classic morphology and was signed as DSRCT. One month after surgery he presented to the ER with nausea, vomiting, and abdominal pain. Physical examination revealed a distended abdomen that was painful upon palpation. Images showed abundant ascitic fluid, multiple peritoneal and omental nodules and diaphragmatic lymphadenopathies. He underwent therapeutic paracentesis, and the fluid was sent to cytology. He was admitted to our institution and...
received palliative care (hydromorphone and midazolam) for a 2 month duration before he died.

Cytospins [Figure 1a-b] and cell block [Figure 1c] were hypercellular, with numerous large, single and pleomorphic cells with an epithelioid appearance, eccentrically located and convoluted nuclei. The cytoplasm was abundant and eosinophilic. The cells showed prominent nucleoli, numerous mitotic figures, and apoptosis. No stroma was identified.

Immunohistochemical studies performed on the cell block showed positivity of the malignant cells with vimentin, epithelial membrane antigen [EMA, Figure 1d], desmin [cytoplasmic, Figure 1e] and cytokeratin AE1/AE3. The tumor cells were negative for calretinin, D2-40 and CK 5-6. The polyphenotypic immunoprofile, in conjunction with the clinical history, confirmed the persistence of DSRCT.

**Discussion**

Desmoplastic small round cell tumor is a rare tumor with aggressive behavior, morphologically the tumor overlaps with other lesions of small cell morphology such as Ewing’s sarcoma, rhabdomyosarcoma, and small cell mesothelioma. These tumors are characterized by reciprocal translocation t(11;22)(p13;q12) that can be confirmed by EWS-WT1 gene fusion transcript by fluorescent in-situ hybridization. In our institution, we did not have the molecular confirmation, but the primary diagnosis was done pretreatment and showed the classic morphology and immunophenotype with divergent differentiation (positive for vimentin, EMA, desmin and AE1/AE3 and negative for calretinin, D2-40 and CK 5-6).

The therapeutic paracentesis showed a hypercellular specimen composed of large single and discohesive cells, with an abundant eosinophilic cytoplasm, perinuclear hoff and frequent mitosis and apoptosis. Due to the lack of groups, stroma and the epithelioid appearance of cells with absence of small cells with high N:C ratio immunocytochemical studies were done on the cell block to rule out reactive mesothelial origin.

There are very few reports that describe the cytological findings of DSRCT tumor after chemotherapy.[1,4] Most of
# Table 1: Summary of cytologic findings for DSRCT on effusions

| References          | Chemotherapy | Type of effusion and cases | Cell size | Nuclei | N:C ratio | Cytoplasm | Architecture | Stroma |
|---------------------|--------------|----------------------------|-----------|--------|-----------|-----------|--------------|--------|
| Crapanzano et al.⁷  | No           | Ascites (2)                | Small (5-7x of a lymphocyte) | Irregular, granular, molding, 3-5 chromocenters, binucleation, occasional apoptosis | Absent | High       | Scant, blue, vacuolated | Hypercellular single cells and occasional loose groups | Absent |
| Ali et al.⁷         | No           | Ascites (1)                | Small     | Large, hyperchromatic, irregular membrane, molding | Absent | High       | Scant       | Hypercellular single cells | Present |
| Bian et al.⁸       | No           | Pleural fluid (1)          | Small     | NA     | NA        | NA        | NA           | Tight groups | +      |
| Chá et al.⁹        | No           | Pleural fluid (1)          | NA        | Pleomorphic, irregular, granular chromatin | Absent | NA        | Scant with well-defined borders | Tight nests | NA |
| Hallman et al.⁸     | No           | Ascites (1)                | NA        | Irregular, monomorphic, hyperchromatic | Absent | NA        | Scant       | Single cells and occasional loose groups | NA |
| Granja et al.¹      | Yes (2), no (1) | Ascites (2) and pleural fluid (1) | NA        | Round or oval | Present | NA        | NA           | Hypercellular single cells and occasional loose groups some with pseudorosette formation | NA |
| Presley et al.⁹     | Yes          | Ascites (1)                | Large     | Irregular membrane, finely granular chromatin, crush artifact, molding | Present | High      | NA           | Single cells and occasional loose groups | Absent |
| González-Arango et al. (present report) | Yes | Ascites (1) | Large | Convoluted, eccentric, with mitosis and apoptosis | Present | Maintained | Abundant and eosinophilic | Hypercellular single cells | Absent |

NA: Not available, DSRCT: Desmoplastic small round cell tumor
the reports describe the usual cytological features of this tumor, including hypercellular aggregates of oval, round or fusiform cells of medium size with a high N:C ratio. The nuclei can show molding, membrane irregularities, granular chromatin, inconspicuous nucleoli, very few mitotic figures and some fragments of metachromatic stroma.\cite{2,4,6} The presence of stroma is crucial to the differential diagnosis; however, it is always necessary to perform immunohistochemical confirmation. DSRCT classically is positive for epithelial, mesenchymal and neural markers and although mesothelium share some markers, studies have demonstrated negativity for D2-40 and CK5-6.

In general, postchemotherapy changes in mesothelial cells have been described as atypia characterized by irregular nuclei, hyperchromasia and prominent nucleoli. The findings of DSRCT in effusions are the same described for fine needle aspiration specimens \cite{1,3,4,7,10}. To our knowledge, only two of these papers were in patients who received chemotherapy and described the loss of cohesion with the hypercellularity, prominent cells size and nucleoli, no mitotic figures and abundant stroma.\cite{1,4}

Herein, we report another case of DSRCT status postchemotherapy, where we found a hypercellular specimen of large single and discohesive cells, as previously described, but in addition to what has been reported, we did not see any presence of stroma, the cells had abundant eosinophilic cytoplasm and there were frequent mitosis and apoptosis.\cite{1,4} Somehow these cells had an epithelioid appearance resembling the reactive mesothelial cells. The immunocytochemical studies performed on the cell block along with the previous clinical history helped to confirm the neoplastic nature of the effusion.

We believe it is important to report unusual morphologic findings in such uncommon tumor due to therapy in order to be able to diagnose recurrence.

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