Desmoplastic Small Round Cell Tumors
Cytologic, Histologic, and Immunohistochemical Features

Fuju Chang, MD, PhD

Desmoplastic small round cell tumor (DSRCT) is a recently recognized clinicopathologic entity that has a predilection for adolescent males and usually affects the abdominal cavity. Due to its uncommon nature, many pathologists lack experience with this tumor. The literature regarding DSRCT is reviewed with special attention to its histologic and cytologic diagnosis. Morphologic features of DSRCT and its immunohistochemical and cytogenetic profile are summarized and differential diagnosis with other small round cell tumors is discussed. As observed by both histologic and cytologic examinations, small round blue cells and fibrosclerotic stroma are the striking morphologic features of DSRCT. The typical immunohistochemical profile is characterized by coexpression of epithelial, mesenchymal, myogenic, and neural markers. Cytogenetically, this tumor harbors a specific karyotypic abnormality, namely (11;22)(p13;q12). These features distinguish DSRCT from other members of the family of small round cell tumors.

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Desmoplastic small round cell tumor (DSRCT) is a rare and highly aggressive neoplasm described as a distinct clinicopathologic entity in 1989 by Gerald and Rosai.1 Most of the cases have been reported in male patients in the second or third decade of life.1–7 These tumors occur mainly in the peritoneal cavity with widespread peritoneal involvement, although other primary sites, such as paratesticular, ovarian, thoracic, lung, intracranial, and head and neck areas have been reported.5,8–14

The literature regarding this tumor is limited and generally comprises case reports.1–14 Practically, DSRCT presents a unique set of diagnostic challenges to histopathologists and cytopathologists because of the similar morphologic appearances of other small round cell tumors. In this mini-review, the cytologic and histologic features of DSRCT as well as its immunocytochemical and cytogenetic profile are summarized, and differential diagnosis with other small round cell tumors is briefly discussed.

CLINICAL FEATURES OF DSRCT

Desmoplastic small round cell tumor is a highly aggressive tumor that predominantly affects young males in their second and third decades of life, with a male-to-female ratio ranging from 2:1 to 5:1.1–14 So far, approximately 200 cases have been reported in the English literature.1–14 These tumors have a tendency to spread along the peritoneum and mesothelial-lined surfaces. It typically presents as a large intra-abdominal mass with numerous smaller peritoneal implants, but has been reported in other body sites including the paratesticular region,8 the pleural serosa,9 the posterior cranial fossa,10 soft tissues and bone,11 the ovary,12 the parotid gland,13 and the lung.14

Common presenting symptoms and signs are abdominal pain, palpable abdominal mass, abdominal distension, and hepatomegaly.5,15,16 Other associated clinical findings are ascites and intraparenchymal liver metastases. Less common findings are retroperitoneal lymphadenopathy, hydronephrosis, bowel obstruction, calcifications, and nodular peritoneal thickening.5,15,16 These symptoms and signs are nonspecific and nondiagnostic. Therefore, it is important to consider DSRCT as a possible diagnosis when a young man presents with nonspecific abdominal symptoms and radiographic evidence of a disseminated, intra-abdominal malignancy.

The development of standard methods for its clinical diagnosis and management has been difficult, because most of our understanding regarding the pathologic and clinical nature of this tumor has been based on case reports and small series of patient studies. The disease is fatal almost uniformly, regardless of the treatment modality used. Surgical resection combined with chemotherapy and radiation may prolong survival in some patients.15,16

PATHOLOGIC FEATURES OF DSRCT

Histologic Features

On gross examination, the tumors are usually large (up to 40 cm in some cases) and are often accompanied by multiple peritoneal implants.2,5,7 Their outer surface is usually bosselated, and the cut surfaces are gray-tan, with areas of necrosis and sometimes with myxoid changes.

Microscopically, the tumor is composed of well-defined nests of small round blue tumor cells separated by abundant desmoplastic stroma (Figure 1, A). The amount of tumor cells versus stroma varies from field to field. In the more desmoplastic areas, tumor cells may be arranged as thin trabeculae or in a single-file fashion. Peripheral pal-
sading of the tumor cells is common in some of the nests. Rosettelike structures may be observed.1-8 Tumor cells are small to medium-sized, with round to oval hyperchromatic nuclei and inconspicuous nucleoli (Figure 1, B). Variable degree of apoptosis and nuclear molding is identifiable, although these changes are less prominent in DSRCT than in small cell carcinoma. Mitotic figures are readily seen. The cytoplasm of tumor cells is usually scanty, and cell borders are indistinct. Eosinophilic cytoplasmic inclusions can sometimes be detected.

The histogenic origin of DSRCT is unclear, although, because of its close association with mesothelial-lined surfaces, it has been suggested that this tumor may be derived from the primitive mesothelium or submesothelial mesenchyme.2

Cytologic Features

The cytology literature regarding DSRCT is limited and generally comprises case reports which include findings in both fine-needle aspiration (FNA) material and ascitic or pleural effusions.17-22 The smears are usually cellular and contain small round cells arranged singly and in clusters with rare mitotic figures (Figure 2, A). Some clusters show rosettelike appearance and others have a 3-dimensional arrangement. Cells demonstrate high nuclear-cytoplasmic ratios, round to oval nuclei containing granular chromatin reminiscent of small cell carcinoma (Figure 2, B). Nuclear molding is also identifiable. The nucleoli are inconspicuous. The cytoplasm is scanty and nonvacuolated. Fragments of hypocellular stroma are often present and appear pink to metachromatic on Diff-Quik and May-Grünwald-Giemsa stains and pale blue on Papanicolaou technique.19-22

Cytological diagnosis of DSRCT could be aided by multiple factors, including a typical clinical presentation and ancillary immunocytochemical and cytogenetic studies. Although histologic examination of a biopsy specimen remains the diagnostic gold standard for DSRCT, cytologic examination on aspirated material and effusion fluid can serve as a mode of preoperative diagnosis in select cases where a biopsy may be difficult to obtain. In addition, cytology procedures are useful in providing follow-up information on tumor remission/recurrence that will impact patient management.
Immunohistochemical and Cytogenetic Features

Immunohistochemically, DSRCT demonstrates a divergent differentiation, a striking feature of this tumor. Typically, tumor cells are immunoreactive for epithelial (keratin and epithelial membrane antigen) (Figure 3, A and B), mesenchymal (vimentin), myogenic (desmin) (Figure 4, A and B), and neural (neuron-specific enolase and CD56) markers. Immunostaining for desmin frequently shows a distinct staining pattern, namely the punctuate and perinuclear cytoplasmic positivity (Figure 3, A and B). Almost all DSRCTs are positive for WT1, a polyclonal antibody against the amino terminus of the WT1 protein. Moreover, antibodies against MIC2 (CD99) antigen can also be positive in DSRCTs, but the staining pattern is usually cytoplasmic, as opposed to the membranous staining observed in Ewing sarcoma/peripheral neuroectodermal tumor (PNET). The desmoplastic stroma of DSRCT stains positive for vimentin and smooth muscle actin (Figure 5).

Ultrastructural findings include the presence of perinuclear whorls of intermediate filaments by electron microscopy, which correspond to the dotlike immunostaining with desmin, together with the absence of specialized...
cell junctions, neurosecretory granules, and long microvilli are pertinent negative ultrastructural findings that also support the diagnosis of DSRCT. In some cases, intraluminal microvillus-like structures, polar cell processes, microtubules, lipid droplets, glycogen, and dense-core granules have been noted.

Cytogenetic studies have demonstrated a characteristic reciprocal chromosomal translocation, t(11;22)(p13;q12), which is different from the t(11;22)(q24;q12) translocation observed in Ewing sarcoma/PNET. The translocation of t(11;22)(p13;q12) is specific for DSRCT, regardless of its anatomic location. The chimeric transcript corresponding to the fusion gene product can be detected by reverse transcriptase-polymerase chain reaction (RT-PCR) technique.

Differential Diagnosis

Histologically and cytologically, DSRCT must be distinguished from other small round cell tumors, such as Ewing sarcoma/PNET, small cell carcinoma, lymphoma, neuroblastoma, Wilms tumor, rhabdomyosarcoma, and malignant mesothelioma.

Like DSRCT, Ewing sarcoma/PNET is composed of small round cells in nests or sheets. Immunohistochemically, Ewing sarcoma/PNET is typically positive for MIC2 (CD99) and vimentin, but negative for cytokeratins and myogenic markers. The characteristic reciprocal chromosomal translocation in Ewing sarcoma/PNET, t(11;22)(q24;q12), involves the long arm of chromosome 11, in contrast to the translocation observed in DSRCT, which involves the short arm of chromosome 11.

Small cell neuroendocrine carcinoma demonstrates many cytologic and histologic similarities to DSRCT, such as small round cells with nuclear molding and absent or inconspicuous nucleoli. Clinically, small cell carcinoma is associated with a much older patient population and usually originates in the lung. On histologic and cytologic examinations, the desmoplastic stroma is not a feature of small cell carcinoma. On immunohistochemistry, small cell carcinoma demonstrates immunoreactivity with epithelial markers, including TTF-1 and neuroendocrine markers, but is negative for myogenic markers such as desmin.

High-grade lymphoma may display cytologic and histologic features similar to DSRCT, but lymphomas often demonstrate a diffuse growth pattern and do not exhibit the cohesion and nuclear features of DSRCT. Immunostains would help with the distinction between the 2 entities by showing reactivity of lymphoma cells to lymphoid markers and negativity to epithelial, neuroendocrine, and myogenic markers.

Moreover, both embryonal and alveolar rhabdomyosarcomas may contain small blue cells arranged in nests or sheets. However, nuclear molding and desmoplastic stroma are not characteristics of rhabdomyosarcoma. Immunohistochemically, rhabdomyosarcoma is positive for muscle markers including desmin, muscle specific actin, and myoglobin, but usually negative for cytokeratins, S100 protein, and neural markers. Neuroblastoma and Wilms tumor also share many morphologic features with DSRCT, but they occur in very young children and cytogenetically lack the specific chromosomal translocation.

CONCLUSION

Desmoplastic small round cell tumor is a rare but well-defined clinicopathologic entity with specific morphologic, immunocytochemical, and genetic features. Clinically, it is a highly aggressive tumor that usually occurs in young adult men, mainly in the peritoneal cavity with widespread peritoneal involvement. Characteristic histologic features of DSRCT include well-defined nests composed of small round cells separated by abundant desmoplastic stroma. Useful cytologic features for diagnosis of DSRCT include high cellularity comprising small round cells arranged singly and in clusters. Tumor cells typically have high nuclear/cytoplasmic ratios, granular chromatin, nuclear molding, and inconspicuous nucleoli. This tumor exhibits a unique immunohistochemical profile, characterized by coexpression of epithelial (keratin and epithelial membrane antigen), neural (neuron-specific enolase and CD56), mesenchymal (vimentin), and myogenic (desmin) markers. The reciprocal chromosomal translocation t(11;22)(p13;q12) is specific for DSRCT, regardless of its site.

By adherence to the clinical information and characteristic cytologic and histologic features of a small round cell population with a unique polyphenotypic immunostaining pattern, pathologists and cytopathologists could reach an accurate diagnosis of DSRCT. For the problematic cases, ancillary techniques such as cytogenetic karyotypic analysis and molecular studies may help in arriving at the correct diagnosis.

References


