Desmoplastic small round cell tumor (DSRCT) is an uncommon and highly aggressive neoplasm that was first described by Gerald and Rosai in 1989 [1]. It has typical clinical, histologic, immunophenotypic, and cytogenetic features that separate it from other small blue round cell tumors, including Ewing's sarcoma (EWS)/primitive neuroectodermal tumor (PNET), embryonal and alveolar rhabdomyosarcoma, neuroblastoma, lymphoma, poorly differentiated carcinoma, Merkel cell carcinoma, and malignant mesothelioma. As aggressive therapy, including multi-agent combination chemotherapy, debulking surgical resection, and radiation therapy, is justified in these patients, an accurate and early diagnosis is crucial. Some authors have reported that an increase in serum cancer antigen 125 (CA 125) might be a specific marker for DSRCT, and thus might permit early diagnosis and therapeutic monitoring of this fast-growing tumor [2,3]. We describe a young male who had intra-abdominal DSRCT and elevated serum CA 125 concentration and briefly review the relevant literature.

Key Words: desmoplastic small round cell tumor, intra-abdominal, CA 125

Desmoplastic small round cell tumor (DSRCT) is an uncommon and highly aggressive neoplasm that was first described by Gerald and Rosai in 1989 [1]. It has typical clinical, histologic, immunophenotypic, and cytogenetic features that separate it from other small blue round cell tumors, including Ewing’s sarcoma (EWS)/primitive neuroectodermal tumor (PNET), embryonal and alveolar rhabdomyosarcoma, neuroblastoma, lymphoma, poorly differentiated carcinoma, Merkel cell carcinoma, and malignant mesothelioma. As aggressive therapy, including multi-agent combination chemotherapy, debulking surgical resection, and radiation therapy, is justified in these patients, an accurate and early diagnosis is crucial. Some authors have reported that an increase in serum cancer antigen 125 (CA 125) might be a specific marker for DSRCT, and thus might permit early diagnosis and therapeutic monitoring of this fast-growing tumor [2,3]. We describe a young male who had intra-abdominal DSRCT and high serum CA 125 concentration. We also discuss the significance of elevated serum CA 125 concentration, and the histogenesis, cytogenesis, and treatment of this tumor.

CASE PRESENTATION

A 29-year-old Taiwanese male presented to another hospital with a 2-month history of abdominal distension associated with constipation, voiding difficulty, and early satiety.
Computerized tomography (CT) scan of the abdomen and pelvis revealed a tumor mass 12 cm in diameter in the pelvic cavity. Colonoscopy and cystoscopy showed external compression of the rectum, sigmoid colon, and urinary bladder. Laboratory studies were unremarkable except for a CA 125 concentration of 882.1 U/mL (normal, < 35 U/mL). Echo-guided needle biopsy was performed and the pathologic diagnosis was PNET.

The patient was transferred to our hospital for further evaluation and treatment. On physical examination, a large, movable, tender mass was palpated in the lower abdomen. On ultrasonography and CT scan, there was a huge lobulated tumor mass between the rectum and the urinary bladder, with severe external compression of the posterior wall of the urinary bladder (Figure 1). In addition, mild ascites, bilateral pleural effusion and multiple nodules in the liver and lung were noted. A series of nuclear medicine studies also showed a high probability of bone metastasis in the left femur, ribs, and mandible. He received combination chemotherapy (dacarbazine, epirubicin, ifosfamide, oncovin), which followed the initial treatment for PNET. After completing six courses of chemotherapy, subsequent CT scan demonstrated shrinkage of the tumor. Serum CA 125 concentration was normalized to 20.7 U/mL and the symptoms subsided gradually. Irradiation over the pelvis and liver was arranged, but the tumor did not show further change. The patient’s serum CA 125 concentration rose again, to 69.8 U/mL. Laparotomy was performed to provide further debulking. However, only excision biopsy was completed because his condition was made inoperable by the presence of many white, firm masses with smooth bosselated surfaces throughout the mesentery (Figure 2) and the parietal peritoneum over the intestine and bladder.

On microscopic examination, various sized, solid nests and cords of small blue round cells were embedded in a hypervascular desmoplastic stroma. The tumor cells were closely packed and had uniform hyperchromatic nuclei with inconspicuous nucleoli and scant eosinophilic cytoplasm (Figure 3). The stroma was dense and collagenous with scattered spindle cells. Areas of calcification were also present. Immunohistochemical studies demonstrated coexpression of cytokeratin, vimentin, desmin, neuron-specific enolase (NSE), and neurofilament. The desmin was in a perinuclear dot-like pattern (Figure 4).

**Figure 1.** Computerized tomography scan of the pelvis shows a huge tumor mass between the rectum and urinary bladder.

**Figure 2.** Many firm masses with smooth and bosselated surfaces over the mesentery.

**Figure 3.** (A) Microscopy shows solid nests of small blue round cells embedded in a desmoplastic stroma (hematoxylin & eosin; original magnification × 8). (B) The tumor cells are closely packed and have uniform hyperchromatic nuclei and scant cytoplasm (hematoxylin & eosin; original magnification × 80).
aggregates of intermediate filaments and cellular junctions. According to these characteristics, the diagnosis was revised to DSRCT. The fusion of the EWS gene on chromosome 22 and Wilms’ tumor suppressor (WT1) gene on chromosome 11, resulting from the chromosomal translocation t(11;22) (p13;q12), was detected by reverse transcriptase polymerase chain reaction (RT-PCR) later at the first hospital.

The patient subsequently underwent another six courses of chemotherapy with a multi-agent regimen (high-dose methotrexate alternating with bleomycin, epirubicin, gemcitabine, and cisplatin) and later received autologous peripheral stem cell transplantation. The main tumor in the pelvic cavity partially responded and there was complete resolution of the hepatic nodules. Unfortunately, recurrence of the tumor in the liver was noted after 6 months and his general condition deteriorated rapidly. Whole liver irradiation was arranged and the epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) gefitinib (Iressa, ZD1839; AstraZeneca UK Ltd, Cheshire, England) was prescribed, but in vain. The patient died of liver failure 26 months after initial diagnosis.

DISCUSSION

DSRCT is a rare neoplasm that has a significant male predilection and usually affects young adults and adolescents. Clinically, the main tumor mass is usually located in the abdomen, pelvis, omentum, or mesentery, with extensive peritoneal involvement. It often spreads diffusely along the intra-abdominal serosal surface, and lacks evidence of a visceral primary site. Rare extra-abdominal sites such as the paratesticular region [4,5], pleura [6,7], central nervous system [8], ovary [9], hand [10], and parotid gland [11] have also been described. The most common complaint of patients is abdominal pain and abdominal distension accompanied by constipation and anuresis due to external compression of the tumor. Metastatic spread and direct implantation into the serosal lining are not uncommon. Histologically, the tumor is typically composed of solid nests of undifferentiated small blue round cells embedded in a desmoplastic stroma. The main diagnostic feature of these tumors is coexpression of epithelial (cytokeratin), mesenchymal (vimentin and desmin), and neural (NSE, neurofilament) markers in the same cell. The most useful diagnostic marker is desmin, which is in a perinuclear dot-like or globoid staining pattern [12]. Ultrastructurally, the tumor cell usually demonstrates paranuclear aggregates of intermediate filament, consistent with the perinuclear dot-like staining pattern of desmin. Secretory lumina, desmosomes, cell processes with microtubules, and electron-dense granules have also been described [12,13]. The clinical manifestations, histology, immunoprofile, and ultrastructural features of our case were consistent with the typical findings of DSRCT.

The histogenesis of DSRCT is uncertain. The consistent immunoprofile and predilection for children and adolescents suggest that it may arise from a primitive pluripotent stem cell with divergent differentiation. The specific cytogenetic abnormality in this tumor, t(11;22)(p13;q12), first noted by Sawyer et al [14], might explain the multidirectional differentiation of the neoplastic cells. This translocation is unique to DSRCT, and the breakpoints involve two chromosomal regions, the EWS gene on 22q12 and the WT1 gene on 11p13. Parkash et al suggested that the divergent differentiation might be the result of EWS-WT1 fusion, allowing a combination of neural differentiation of Ewing’s sarcoma with the multidirectional differentiation of Wilms’ tumor [7]. In addition, the fusion protein appears to induce expression of platelet-derived growth factor A, a potent fibroblast growth factor that could contribute to the desmoplastic stroma formation [15]. Detection of the transcript by RT-PCR is a helpful method to confirm diagnosis of the tumor [16].

CA 125 is a high molecular weight glycoprotein. Serum CA 125 concentration has been shown to be elevated in cases of ovarian, pancreatic, breast, colon, lung, and endometrial carcinoma. Several reports have described an increase in serum CA 125 concentration in patients with DSRCT [2,3,9,17]. Whether the high serum CA 125 concentration is attributable to the tumor cells themselves or to
the mesothelial expression of this antigen is a matter for argument. In our case, there was a high serum CA 125 concentration, and normalization occurred together with decreased ascites and shrinkage of the tumor mass after chemotherapy. Re-elevation of the concentration was subsequently noted when the tumor grew again. So, CA 125 could be a useful marker for DSRCT and could allow the clinician to monitor treatment progress.

The initial pathologic diagnosis in our case was PNET at another institution and the first chemotherapy regimen was that for PNET. We propose that CA 125 could be a marker for DSRCT. Genetic testing could be used earlier for small round cell tumors of unknown origin with elevated CA 125. If genetic testing identifies the unique findings of DSRCT, treatment can be started promptly.

DSRCT is a highly aggressive neoplasm with an extremely poor prognosis. Complete excision of the tumor is often impossible due to multiple tumor implants in the peritoneum, and patients usually die of the disease and widespread metastasis, with a median survival of 17 months from diagnosis [18]. Survival may be improved by high-dose multi-drug combination chemotherapy followed by aggressive surgical resection, radiotherapy, and myeloablative chemotherapy with stem-cell rescue [19–21]. Recently, gefitinib (Iressa, ZD1839), an orally active, selective EGFR-TKI that blocks signal transduction pathways involved in the proliferation and survival of cancer cells, has been developed. Preclinical studies demonstrate that gefitinib is a promising agent for the treatment of a wide range of tumors, including non-small-cell lung cancer, prostate, breast, head and neck, gastric, and colorectal tumors, and has additive-to-synergistic effects when combined with radiation or chemotherapy in various cell lines and xenografts [22]. No clinical data on the use of gefitinib in the treatment of DSRCT have been reported. This agent was prescribed in our case, but to no avail. Further investigation is needed.

The specific cytogenetic features of DSRCT raise the possibility of monoclonal antibody-based therapy without significant toxicity to normal tissues. Although detection of the EWS-WT1 chimeric transcript is specific for DSRCT, its potential use in detecting minimal residual disease in blood or bone marrow has not been addressed in published reports. Modak et al described GD2, which is recognized by the monoclonal antibody 3F8, and a novel tumor antigen recognized by the monoclonal antibody 8H9 as two possible targets for immunotherapy of this tumor [23]. GD2 is a disialoganglioside that is widely expressed among neuroectodermal tumors as well as adult sarcomas; 8H9 recognizes a 58 kd surface antigen expressed among neuroectodermal, mesenchymal, and epithelial tumors, with restricted expression in normal tissues. Using immunohistochemistry, 70% of DSRCTs were reactive to 3F8 and 96% to 8H9 in their study, and both GD2 and the 58 kd antigen were localized to tumor cell membrane and stroma. As a result, monoclonal antibodies selective for cell surface tumor-associated antigens may be useful for diagnosis and therapy of minimal residual disease, as recently demonstrated in advanced-stage neuroblastoma.

In summary, the clinician should be alert to the possibility of DSRCT when young men present with huge peritoneal tumor masses without relation to a particular organ. Pathologists must keep this entity in mind and make the correct diagnosis by performing specific immunohistochemical, ultrastructural, and cytogenetic studies.

**REFERENCES**


