Desmoplastic Small Round-Cell Tumor: An Adult with Previous Exposure to Agent Orange

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Desmoplastic small round-cell tumor is an uncommon, highly aggressive tumor with a predilection for pediatric age groups and young adults. It is very unusual in the elderly population. Although Agent Orange has been associated with soft-tissue sarcoma, an association with desmoplastic small round-cell tumor has not been reported. A 52-year-old male presented with abdominal distention, dyspnea, and a 9 kg weight loss. Prior history was significant for hepatitis C and diabetes. He was a Vietnam veteran and he admitted being exposed to Agent Orange. On physical examination, the abdomen was distended and tense. Computed tomography scan of the chest, abdomen and pelvis demonstrated extensive mediastinal and retroperitoneal adenopathy, diffuse omental masses and extensive pleural, intra-abdominal and pelvic ascites. Omental core needle biopsy was consistent with desmoplastic small round-cell tumor based on morphology and immunohistochemistry. He responded poorly to chemotherapy with high-dose cyclophosphamide, doxorubicin and vincristine and died 5 months after presentation secondary to neutropenic sepsis despite G-CSF support and antibiotics.

Key words: desmoplastic – sarcoma – Agent Orange

INTRODUCTION

Desmoplastic small-round cell tumor (DSRCT) is an uncommon, highly aggressive tumor with a predilection for pediatric age groups and young adults. It is very unusual in the elderly population. Although Agent Orange has been associated with soft-tissue sarcoma, association with DSRCT has not been reported.

CASE REPORT

A 52-year-old male presented with a 3–4-week history of abdominal distention and discomfort, accompanied by a 20 lb weight loss. His past medical history included hepatitis C (treated with interferon), anxiety, diabetes mellitus and kidney stones. The patient was a Vietnam veteran and a marine soldier in the corps. He was sprayed and exposed to Agent Orange by inhalation and skin contact on a daily basis for 8 months. He was a former smoker and reported no alcohol or drug use. On physical examination, there was remarkably decreased air entry at both lung bases. His abdomen was distended and tense with the presence of shifting dullness. A mass of at least 10 cm was palpable in the left upper quadrant. He had no hepatosplenomegaly or peripheral lymphadenopathy. Laboratory work-up was unremarkable except for CA 125 of 641 U/ml. A CT scan of the chest (Fig. 1), abdomen and pelvis (Fig. 2) demonstrated extensive mediastinal and retroperitoneal adenopathy, diffuse omental masses and extensive pleural, intra-abdominal and pelvic ascites. CT-guided 18-gauge core biopsy of the omental mass showed a cellular proliferation of uniform small round cells involving fibroadipose stroma without apparent areas of necrosis (Fig. 3). Immunohistological studies were positive for desmin in a dot-like pattern.
epithelial membrane antigen (EMA), vimentin, CD 99 with cytoplasmic immunoreactivity and focally positive for synaptophysin while negative for myogenin, CAM 5.2/AE1/AE3 and chromogranin. The overall results demonstrate overlapping immunophenotypes between DSCRT and Ewing sarcoma/primitive neuroectodermal tumor. However, the presence of desmoplasia within the tumor and the clinical presentation supported the diagnosis of DSCRT. The slides were reviewed by the Department of Pathology at Memorial Sloan-kettering Cancer Center, New York, New York. They concurred with our diagnosis, and they suggested immunostaining for WT1 but there was insufficient tissue. RT-PCR to detect chromosomal abnormalities could not be performed because of scant tissue as well. The patient was treated according to the P6 protocol (Courses 1, 2, 3 and 6 consisted of HD-CAV, high-dose cyclophosphamide 2100 mg/m²/day on days 1 and 2, doxorubicin 75 mg/m²/day and vincristine 2.0 mg/m²/day on days 1, 2 and 3. Courses 4, 5 and 7 consisted of ifosfamide 1.8 g/m²/day and etoposide 100 mg/m²/day for 5 days). He received only one cycle of HD-CAV but responded poorly and died 5 months after presentation secondary to neutropenic sepsis despite G-CSF support and antibiotics.

DISCUSSION

DSRCT is a rare aggressive sarcoma that occurs predominantly in male adolescents or young adults (1). Median age at diagnosis is 21.7 years. Most tumors are confined to the abdomen. The liver, lung and bone marrow are common sites of metastases (2). DSRCT presents a unique set of diagnostic challenges to histopathologists and cytopathologists because of the similar morphologic appearances of other small round-cell tumors (Ewing sarcoma, rhabdomyosarcoma, lymphoma, primitive neuroectodermal tumor, neuroblastoma, Wilms tumor). Microscopically, nests of small round cells with hyperchromatic nuclei and scanty cytoplasm are embedded in a desmoplastic stroma, a key diagnostic feature. Immunohistochemically, the tumor cells are immunoreactive for epithelial (keratin and EMA), mesenchymal (vimentin), myogenic (desmin) and neural (neuron-specific enolase and CD56) markers (3). Moreover, antibodies for MIC2 (CD99) antigen can be positive in DSRCTs, but the staining pattern is usually cytoplasmic, as opposed to the membranous staining observed in Ewing
In addition, DSRCTs have a characteristic dot-like staining pattern with desmin on immunohistochemistry. In our case, the tumor cells were positive for vimentin, desmin in a dot-like pattern, EMA and CD99 with a cytoplasmic staining pattern, these findings support the diagnosis by showing reactivities to epithelial, myogenic and neural markers. Genetically, a unique chromosomal translocation t(11;22)(p13;q12) has been identified, which results in the fusion of the Ewing sarcoma gene with the Wilms tumor gene. Multimodal therapy consisting of aggressive surgical debulking and systemic chemotherapy (cyclophosphomide, doxorubicin and vincristine interspersed with ifosfamide, etoposide) with or without radiotherapy have shown survival benefit. Agent Orange, so-called from the orange color of its storage drums, is a defoliant phenoxy herbicide mixture used during the Vietnam War to destroy forests in Vietnam. The USA sprayed 77 million liters of Agent Orange over forests in Vietnam, and as a result, members of the Armed Forces were exposed to it. As the US veteran population ages, study results continue to emerge. It is probable that damage to humans would be due to the highly toxic impurity dioxin, present in Agent Orange. It is considered a mutagen, and teratogen in plants and animals but so far no consistent pattern of chromosomal anomalies has been observed in humans. The strongest evidence for an association between soft-tissue sarcoma and exposure to phenoxy herbicides came from case–control series and other cohorts from Sweden. However, the data have not been consistent in determining an association of Agent Orange to cancer. Yet, the 2002 update of the National Academy of Science concluded that there is ‘sufficient evidence’ of an association between exposure to Agent Orange and STS, non-Hodgkin lymphoma, Hodgkin lymphoma, chronic lymphocytic leukemia and prostate cancer. Occurrence of DSRCT in the adult population is extremely rare. Reporting this case should raise awareness of this rare entity in an unusual age group. Despite this rarity, DSRCT should also be considered in the differential diagnosis of intra-abdominal malignancies in older individuals. Although there is no direct evidence to link Agent Orange to this type of sarcoma, a detailed occupational history and probably correlation with cytogenetics is warranted to unfold more cases that might be related to exposure to Agent Orange or other carcinogens.

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Conflict of interest statement

None declared.

References