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Demsoplastic Small Round Cell Tumor:a Diagnostic and Therapeutic Dilemma

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ABSTRACT

Desmoplastic small round cell tumor (DSCRT) is a rare variant of sarcoma with a highly aggressive behavior. It usually affects abdominal cavity and has a male predominance. Its correct diagnosis and treatment is sophisticated and requires an experienced multidisciplinary team. Hereby we present a 25 yrold man from Kerman Province in 2013 with abdominal mass and ascites who underwent sonograghy guided percutaneous needle biopsy which was misleading and inconclusive for diagnosis. Thus an open biopsy was fulfilled which revealed solid nests of small round cells with hyperchromatic nuclei and clear cytoplasm surrounded by a desmoplastic stroma suggestive for DSCRT. The diagnosis was confirmed by positive immunohitochemical reaction for cytokeratin, desmin and neuron specific enolase(NSE).Ultimately the patient underwent chemotherapy on the basis of P6 protocol without surgical debulking.Diagnosis and treatment of DSCRT could be a dilemma due to its rarity, various clinicopathologic mimickers and lack of a consensus about its management.

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Introduction

Desmoplastic small round cell tumor (DSCRT) is a rare and highly aggressive neoplasm defined as a distinct clinicopathologic entity in the last decade of twentieth century. More than 200 cases have been reported till now but the exact incidence of this rare tumor have not been clarified so far (1).

DSCRT usually occur in adolescents and young adults with a male predominance (male to female ratio 4:1) (2). It manifests as vague abdominal or pelvic discomfort and less commonly as a palpable abdominal mass (3) DSCRT is also an extremely rare cause of ascites which mandates a proper approach to uncommon causes of ascites (4). Liver and lung can be involved secondarily as metastatic disease. Involvement of other organs such as testes, ovaries and pleura has been reported (5).

DSCRT diagnosis is primarily established on

the basis of radiologic and histological features but it is confirmed by immunohistochemistry and cytogenetic study due to the large number of differential diagnoses (6). No optimal treatment has been introduced for this malignancy, however multiagent chemotherapy, surgical debulking and radiotherapy are current modalities utilized (7).

Due to uncommon nature of this tumor, we present a 25 yr old man with inta-abdominal DSCRT to share their experience concerning its challenging diagnosis and treatment with a more emphasis on histopathological diagnosis and its possible caveats such a false negative result of percutaneous needle biopsy.

Case Presentation

Patient was a 25 yr old man from Kerman Province in 2013 with abdominal pain in his hypogastric, periumblical and suprapubic area radiating to his back. Abdominal discomfort had been started 3 days before his admission. On physical examination the abdomen was a little distended and an irregular mass was palpable in periumbilical area. Bowel sounds were auscultated and seemed normal. All laboratory tests (complete blood count, electrolytes, blood urea nitrogen, creatinine and amylase) were in normal range except a slightly elevated liver enzymes (Aspartate aminoteransferase = 68 IU/L and Alanine aminoteransferase =53 IU/L ; normal range = 5-40 IU/L).

Abdominal sonograghy revealed a heteroechoic mass at supravesical and umbilical level con-

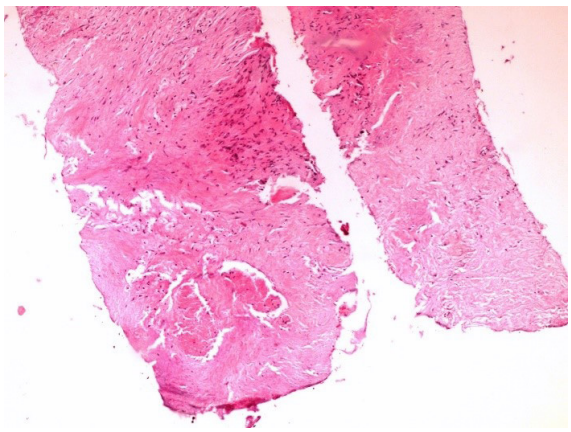

Fig. 1
Percutaneous needle biopsy of intra-abdominal mass revealed foci of tumoral necrosis along with fibroblasic proliferation (Hematoxylin and Eosin x100)

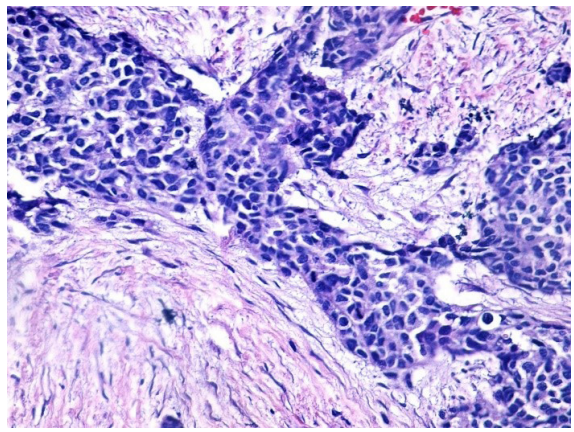

Fig. 2
Open wedge biopsy of intra-abdominal mass depicted well defined nests of small cells with hyperchromatic nuclei surrounded by fibroblasts (Hematoxylin and Eosin x400)

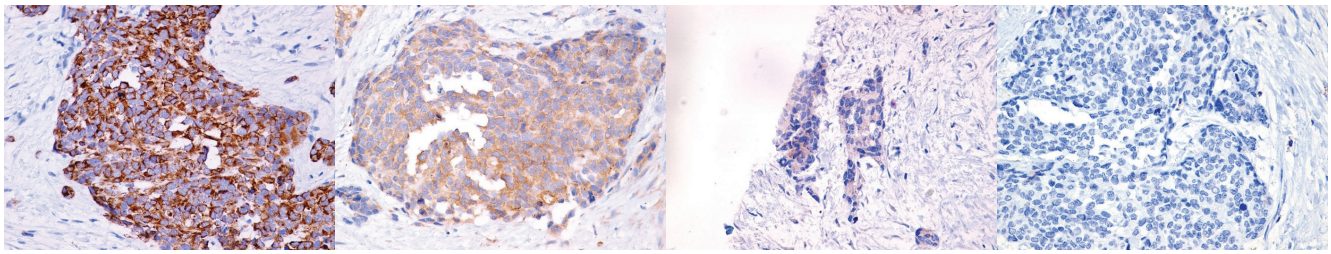

Fig. 3
Immunohistochemistry panel. a) Characteristic perinuclear punctuate staining for desmin(counterstained by Hematoxylin x400). b) Positive cytoplasmic reaction for NSE (counterstained by Hematoxylin x400). c) Positive reaction to cytokeratin in tumoral cells (counterstained by Hematoxylin x400). d) Negative reaction to CD45 (counterstained by Hematoxylin x400).

sisting of hypoechoic and echogenic areas. There were also target shape lesions in liver in favor of metastasis. Computed tumography showed a heterodense soft tissue mass in the lower abdomen and retrovesical space without an obvious relation to intra-abdominal organs along with small amount of ascites and radiologic impression of a malignant process was made.

On next step, the patient underwent percutaneous needle biopsy under sonograghy guide. The histopathologic picture revealed a neoplastic growth composed of fibroblastic proliferation with focal necrosis (Fig. 1). At first glance, impression of fibromatosis struck our mind. Nevertheless, radiologic discrepancy and presence on necrosis made us recommend an open biopsy. On laparatomy, many peritoneal seedings and a large retrovesical mass with extension to retrosigmoidal space was explored. There was a small amount ascites measuring 300 mlin abdominal cavity. Histological evaluation of tumoral mass wedge biopsy revealed solid nests of small round cells with hyperchromatic nuclei and clear cytoplasm surrounded by fibroblasts and a desmoplastic stroma (Fig. 2). Thus, diagnosis of DSCRT was suspected, so immunohistochemistry study was requested to confirm the diagnosis. Immunohistochemistry results exhibited positive reaction for cytokeratin, desmin and neuron specific enolase(NSE) along with a negative reaction for CD99 and CD45 (Fig. 3). Finally the patient was referred to an oncologist with definite diagnosis of DSCRT and underwent chemotherapy according to P6 protocol.

After receiving Ethical Committee agreement and patient's informed consent, the case clinical data were gathered and written.

Discussion

DSCRT is a member of "small blue round cell tumor" including neuroblastoma, malignant lymphoma, rhabdomyosarcoma, Wilm's tumor and peripheral neuroectodermal tumor (PNET) (8). This entity is discriminated from other small blue round cell tumors by its epithelial, neural and mesenchymal differentiation (9,10). DSCRT is highly aggressive tumor considered as a separate entity (3). Patients' age with this malignancy ranges from 6-49 yrwith the mean age of 22 yr. Male sex is involved predominantly with male to female ratio of 4:1(10).

Clinical presentations of DSCRT include: abdominal pain, abdominal distension, palpable abdominal mass and hepatomegaly (11). Ascites and intraparanchymal liver metastasis are also other associated findings. In the present case, small amount of ascites was detected by sonograghy and evaluated around 300 ml during laparatomy. In a similar case, ascites of unknown etiology was the main presentation of DSCRT in 74 yr old man. It had a low serum ascites albumin gradient (8 g/l) suggesting a non-portal hypertension cause. Moreover, malignant ascites occurs in advanced or recurrent malignancies. Peritoneal carcinomatosis with concomitant ascites can be developed as a consequence of urinary bladder, ovary, colon, stomach and pancreas malignancies. DSCRT has rarely been reported as the underlying cause of malignant ascites (4,12).

Less common manifestations of DSCRT are retroperitoneal lymphadenopathy, hydronephrosis, bowel obstruction, calcification and nodular peritoneal thickening (13). Anyhow, these symptoms are neither specific nor diagnostic for this tumor. Therefore, consideration of DSCRT as a possible diagnosis in a young man with nonspecific abdominal symptoms and a disseminated intra-abdominal malignancy seems logical (11).

CT scan with intravenous contrast is the most useful radiologic modality for initial diagnosis and follow-up. The most common feature of DSCRT in CT scan is multiple intrapeitoneal soft tissue masses without a distinct organ of

origin. The tumor usually originates from retrovesical space. Foci of low attenuation and low enhancement are common findings and represent necrosis, hemorrhage and fibrous components. Primary tumor and metastatic deposits can also show foci of calcification (3). Nodular peritoneal thickening due to peritoneal sarcomatosis, liver metastasis, small volume ascites, lymphadenopathy, bowel and urinary obstruction are other radiologic features documented previously (2). In the present case, retrovesical origin of tumor and absence of relation with intra-abdominal organs were helpful radiologic clues for DSCRT diagnosis. Sonograghy is another useful radiologic modalityfor percutaneous biopsy of superficial masses which are typically demonstrated as lobulated heterogenous hypo-echoic lesions (1).

Radiologic differential diagnosis of DSCRT is broad and encompasses various neoplastic inflammatory and miscellaneous processes especially diffusely spreading entities like desmoids tumor, lymphoma, malignant peritoneal mesothelioma, peritoneal sarcomatosis, tuberculosis and gastrointestinal stromal tumor (14).This diagnostic dilemma was evident in our case because the needle biopsy resembled fibromatosis at first glance.

Histological examination of a biopsy specimen remains gold standard for diagnosis of DSCRT. Nevertheless, percutaneous needle biopsy might yield inadequate tumor samples and mislead to another diagnosis due to its large amount of desmoplasia. This problem occurred in our case and another onewhich underwent rebiopsy to provide enough specimens for ancillary tests such as molecular study (15). Thus open tumor biopsy via laparatomy can provide enough specimens especially in suspicious cases.

Histopathologically, the tumor is composed of well defined solid nests of small round cells with hyperchromatic nuclei surrounded by desmoplastic stroma consisting of fibroblasts and hyperplastic blood vessels (6). It must be distinguished from other small blue round cell tumors. Immunohistochemistry plays a pivotal role on confirmation of DSCRT and its discrimination from other small blue round cell tumors. DSCRT demonstrates characteristic polyphenotypic differentiation toward epithelial (keratin and epithelial membrane antigen), mesenchymal (vimentin), myogenic (desmin), and neural (neural specific enolase and CD56) elements (8,11). This polyphenotypic differentiation was depicted elegantly in this case via positive reaction for cytokeratin, desmin and neuron specific enolase (NSE). In spite of morphologic similarity of lymphomas to DSCRT; they demonstrate diffuse growth pattern and lack cohesion and nuclear features in DSCRT. Reactivity to lymphoid markers and negativity to epithelial, neuroendocrine and myogenic markers make a distinction between lymphoma and DSCRT (16). Ewing's sarcoma also resembles DSCRT and consists of nests and sheets of small round cells, but they are immunohistochemically different. Unlike DSCRT, Ewing's sarcoma is negative for cytokeratin and myogenic markers. Other similar tumor to DSCRT is small cell carcinoma. Nevertheless, it is more common older patients, originates from lung and lack desmoplastic stroma. On immunohistochemistry, it reacts with TTF1 and neuroendocrine markers. Moreover, in young children, rhabdomyosarcoma, Wilm's tumor and neuroblastoma fall in differential diagnosis category of DSCRT. Rhabdomyosarcoma is positive for desmin, muscle specific markers and myoglubin but negative for S100, neural markers and cytokeratin. Wilm's tumor and neuroblastoma lack the specific chromosomal translocation of DSCRT that is t (11;22)((p13;q12) and differs from t(11;22)(q24;q22) in Ewing's sarcoma(11).

Recently, a new staging system has been suggested by MD Anderson Cancer Center for DSCRT. This system is based on peritoneal cancer Index (PCI), presence of liver metastasis and extra-abdominal metastasis. Such a staging system is required for proposing and comparing

various therapeutic strategies (5,11).

There has been no consensus on DSCRT treatment due to its rarity so far. Three modalities have been suggested by different authors including chemotherapy, aggressive debulking surgery and chemotherapy. Kushner et al. applied a multiagent chemotherapy called P6 protocol. This protocol consists of seven courses of chemotherapy (four courses of HD-CAV, high dose cyclophosphamide 2100 mg/m2/d on days 1 and 2, doxorubicin 75mg/m2/d and vincristine 2mg/m2/d on days 1,2,3 and three courses of ifosfamide1.8 g/m2/d and etoposide 100 mg/m2/d for 5 days) (7).Hayes Jordan et al. introduced a new anthracyclin based therapy regimen for recurrent diseases (1). Goodman et al. used abdominopelvic irradiation after debulking surgery and chemotherapy and observed a median survival of 32 months (17).

Conclusion

Diagnosis and treatment of DSCRT might be challenging due to its rarity and various clinicopathologic mimickers. Therefore, clinician and pathologists should be familiar to its features to manage it properly.

Acknowledgements

The authors declare that there is no conflict of interests.

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