Clinical Case Reports

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CASE REPORT

Diagnosis of desmoplastic small-round-cell tumor by cytogenetic analysis: a case report

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Key Clinical Message

We herein present atypical histologic and immunohistochemical features of DSRCT. The various differential diagnoses of DSRCT may occasionally generate confusion. Cytogenetic analysis may solve diagnostic dilemmas such as that in our case. Further studies are required to establish a standard treatment for DSRCT.

Keywords

Chromosomal translocation, cytogenetic analysis, diagnostic dilemma, desmoplastic small-round-cell tumor.

Introduction

Desmoplastic small-round-cell tumor (DSRCT) is a rare, highly aggressive intra-abdominal neoplasm with an extremely poor prognosis, first described in 1989 [1]. It frequently occurs in the abdominal cavity and pelvis with an undetermined histologic origin, and its incidence in males (>80%) and females differs [2–6]. In one comprehensive study, the typical immunohistochemical features were epithelial marker positivity (cytokeratin, 91%; epithelial membrane antigen [EMA], 88%), mesenchymal marker positivity (desmin, 91%; vimentin, 84%), and various results for neural antigens [6]. Atypical histologic and immunohistochemical features can pose a diagnostic dilemma. We herein report a case of epithelial marker – negative DSRCT, only a few cases of which have been reported worldwide. Cytogenetic profiles could provide useful diagnostic information in such cases.

Case Report

A 22-year-old woman (gravida 0, parity 0) presented with abdominal distension. A physical examination revealed a bulky abdominal tumor. Magnetic resonance imaging showed a mass in the pelvic cavity, and computed tomography showed a large, complex, heterogeneously enhancing mass invading the abdominal cavity and displacing the ovary, colon, and small intestine (Fig. 1). The serum CA-125 level was elevated at 285.3 U/mL (normal, <35 U/mL). The serum CA19-9, carcinoembryonic antigen, and alpha-fetoprotein levels were within the normal range.

Probe laparotomy only with tumor biopsy was performed to determine the diagnosis. During laparotomy, the mass appeared soft and immobile, nontender, and very vascular (Fig. 2). Immediately after laparotomy, the patient presented with acute progression of symptoms such as ascites and pelvic and abdominal tenderness. Early

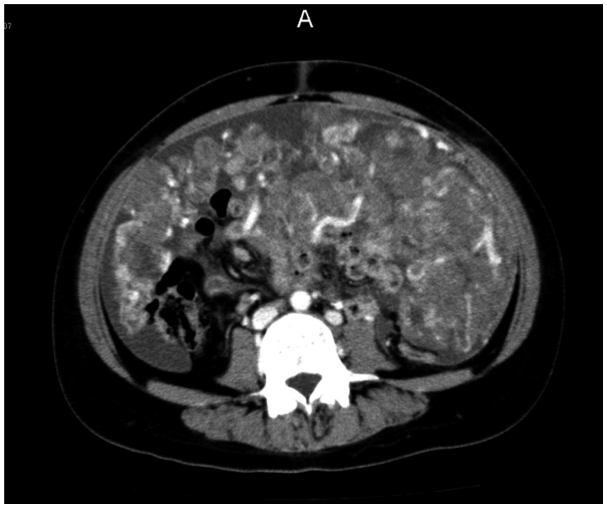

Figure 1. Computed tomography shows a large heterogeneously enhancing mass invading the abdominal cavity.

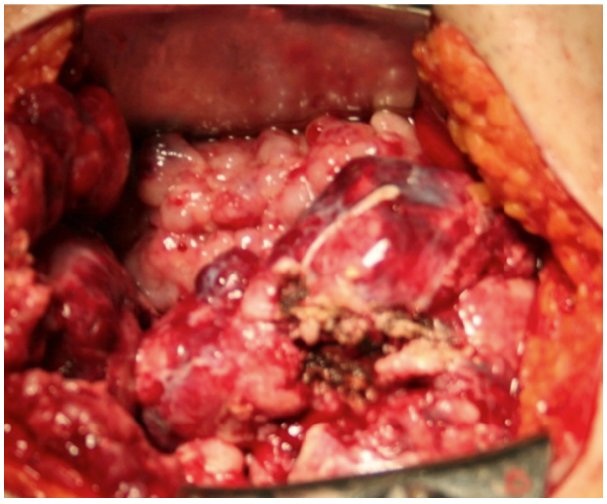

Figure 2. Intraoperative image of the multilobulated mass.

therapeutic intervention, without waiting for pathological examination of a biopsy specimen, was necessary for this patient. Frozen biopsy was performed, and the results were suspicious for a mesenchymal tumor; therefore, the patient underwent chemotherapy with doxorubicin and ifosfamide.

A pathological examination showed diffuse infiltration with a necrotic area of short spindle cells and small round cells with irregular nuclei (Fig. 3A). The mitotic rate was high (60 per 10 HPF).

Immunohistochemical analysis was performed using antibodies directed against epithelial markers (EMA, cytokeratin 7, cytokeratin 20, CAM5.2, and AE1/3), mesenchymal markers (desmin and vimentin) (Fig. 3B,C), and neural markers (synaptophysin and s-100 protein). Unfortunately, the atypical immunohistochemical features made diagnosis of this tumor difficult. The tumor cells were positive when stained with antibodies to EMA, vimentin, desmin, and synaptophysin, but were negative for s-100 protein and some epithelial markers (cytokeratin 7, cytokeratin 20, CAM5.2, and AE1/3).

Cytogenetic analysis was necessary for a definitive diagnosis in this case. In our case, detection of the chromosomal translocation t(11;22)(p13;q12) allowed for diagnosis by fluorescence in situ hybridization [7] and polymerase chain reaction (PCR).

PCR revealed fusion of the Ewing sarcoma gene (*EWS*) and Wilms tumor gene (*WT1*), and break-apart FISH detected translocations in the *EWS* gene (Fig. 4A,B). PCR and FISH were carried out according to the manufacturer's instructions, as described previously [8, 9].

The patient underwent treatment with five cycles of VDC regimens (vincristine, doxorubicin, and cyclophosphamide) and three cycles of VAC regimens (vincristine, actinomycin D, and cyclophosphamide) after we established the definitive diagnosis. However, the patient's disease progressed throughout all three cycles of VAC regimens, and she died of her disease 9 months after her initial diagnosis.

Discussion

The differential diagnosis of small round cell tumor includes Ewing sarcoma, embryonal rhabdomyosarcoma, Wilms tumor, neuroblastoma, medulloblastoma, synovial sarcoma, and lymphoma; these tumors are often confused with one another [10]. A diagnosis of DSRCT is usually made by a combination of the histologic appearance and immunohistochemical staining results. Therefore, atypical histologic and immunohistochemical features can pose a diagnostic dilemma. Generally, DSRCTs show the typical histologic features of a large necrotic area, sharply demarcated nests of small round cells, or spindle cells embedded in a desmoplastic stroma. The small nests of cells are variably sized and contain hyperchromatic nuclei with faintly eosinophilic, scanty cytoplasm [3, 11–13]. Most DSRCTs coexpress epithelial markers (cytokeratin, EMA), mesenchymal markers (desmin, vimentin), and neural markers (synaptophysin, s-100 protein) [3]. In our case, however, immunohistochemical staining disclosed negativity for some epithelial markers (cytokeratin 7, cytokeratin 20, CAM5.2, and AE1/3) and EMA positivity. In contrast, expression of mesenchymal markers (desmin and vimentin) was positive. In particular, the desmin positivity made it possible to diagnose a malignant myometrial tumor. Embryonal rhabdomyosarcoma, synovial sarcoma, ES/PNET, and an unusual type of leiomyosarcoma should be

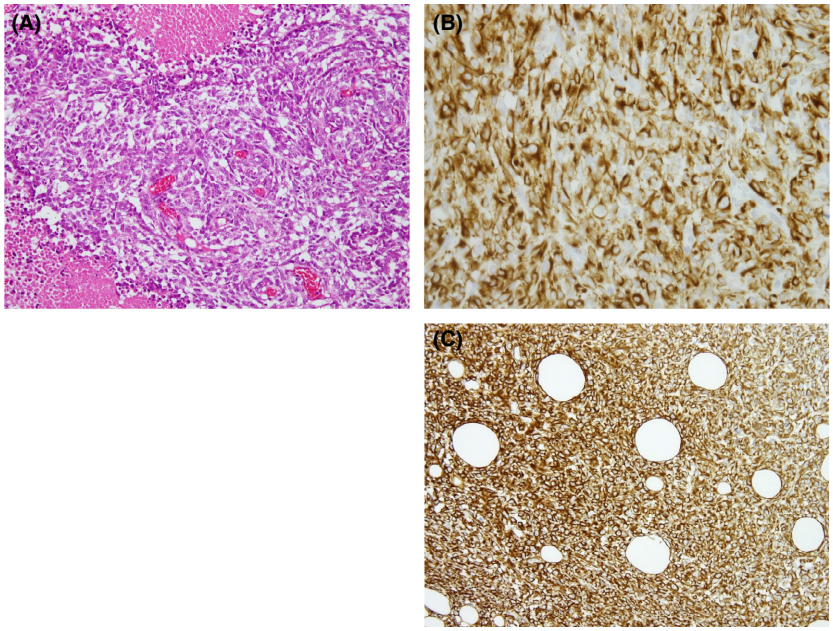

Figure 3. (A) The tumor shows diffusely infiltrating short spindle cells and small round cells (×200). (B) Immunohistochemical staining for desmin shows a dot-like perinuclear reaction in the tumor cells (×400) and (C) positive staining with vimentin (×200).

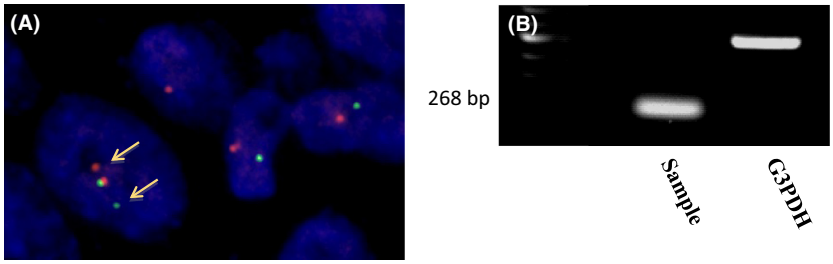

Figure 4. (A) Fluorescence in situ hybridization using a break-apart probe for the Ewing sarcoma breakpoint region 1 gene is positive. (B) *EWS/WT1* rearrangement reverse-transcription PCR demonstrates the 268-bp product.

considered in such cases. The exact histogenesis was unclear in the present case.

Definitive diagnosis was achieved in our case by cytogenetic analysis. DSRCT is generally characterized by a chromosomal translocation t(11;22)(p13;q12) that results in the fusion of the genes *EWS* and *WT1* [7, 11, 13–15].

DSRCTs that are negative for epithelial markers are relatively rare, and only three such cases have been reported. Cytogenetic analysis may resolve diagnostic dilemmas such as that in our case [11, 16, 17].

With respect to treatment of DSRCT, chemotherapy with an intensive alkylator-based regimen is associated with better survival than is standard-dose chemotherapy. This regimen has a risk of toxicity that requires intensive transfusions and antibiotic support [4, 18]. Complete surgical resection is also associated with improved survival. However, debulking surgery is usually impossible at an advanced stage [4, 19, 20]. Despite such aggressive therapy, the outcome is poor. In one study, 25 of 35 patients died of widespread metastases within a mean of 25.2 months from the time of their diagnosis [21]. Although our patient received chemotherapy using VDC and VAC, she finally died of local tumor progression.

Our patient presented with atypical histologic and immunohistochemical features of DSRCT. The various differential diagnoses of DSRCT may occasionally generate confusion. Cytogenetic analysis may solve diagnostic dilemmas such as that in our case. Further studies are required to establish a standard treatment for DSRCT.

Conflict of Interest

None declared.

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