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Intra-Abdominal Desmoplastic Small Round Cell Tumor

- Immunohistochemical and ultrastructural study -

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= Abstract = **We report a case of malignant intraabdominal tumor in a 14 years old Korean girl that presented with abdominal pain, distension and palpable mass. Emergency laparotomy revealed bulky peritoneal masses with numerous satellite implanting nodules. Light microscopically the tumor was characterized by discrete islands of compact, small epithelium-like cells encased in desmoplastic stroma. Immunohistochemically the neoplastic cells expressed vimentin strongly and diffusely and also neuron specific enolase strongly and focally. Ultrastructurally the neoplastic cells showed whorled intermediate filaments, a fair number of mitochondria, dilated rough endoplasmic reticulum, a few fat vacuoles and zonula-adherens type junctions. However there was no evidence of specific differentiation. Histologic, immunohistochemical, and electronmicroscopic observations indicated a primitive malignant neoplasm simultaneously expressing mesenchymal and neural differentiation. Our case did not express any epithelial markers including pancytokeratin, epithelial membrane antigen and CAM 5.2.**

Key words : *Small round cell tumor, desmoplastic, abdominal, children, immunohistochemical study, ultrastructural study,*

INTRODUCTION

"Intraabdominal desmoplastic small cell tumors with divergent differentiation" is a recently described and rare clinicopathologic entity. Gerald and Rosai (1989) firstly described bulky peritoneal tumors occurred in children and invariably displaying nests of small cells set in a dense fibromyxoid stroma. Ordonez et al. (1989) also reported similar case in a 28 year-old male and there were several more reports (Swanson et al., 1988; Gonzalez-Crussi et al., 1990). Clinically, this tumor is characterized by occurring in children or adolescence, predominant or exclusive intraabdominal location, their large size, peritoneal dissemination mimiking metastatic nature but the absence of an apparent primary site. Histopathologically, this tumor is a primitive small round cell malignancy of uncertain histogenesis capable of simultaneously expressing epithelial, mesenchymal, and less consistently, neural phenotype by immunohistochemical and eletronmicroscopic observation. This tumors showed a male predominance and male to female ratio was 5 to 1 (Gerald et al., 1991). In Korea, still no reported case was found, therefore, we report a typical case of intraabdominal desmoplastic small cell tumor with clinicopathologic, immunohistochemical and ultrastructural study.

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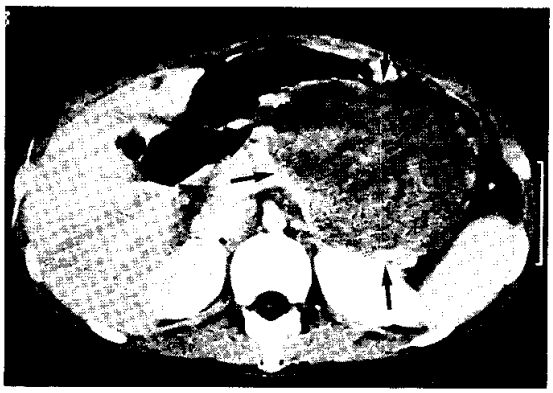

Fig. 1. Abdominopelvic computerized tomogram revealed that a huge mixed dinsity mass was seen at the abdominal cavity, measuring about 12.0×9.0cm in cross, which was not sepatable from pancreatic body and tail. The mass displaced stomach to the anterior right side. Superiorly, the mass extended to the fundus of stomach, and inferiorly, to the entire mesenteric area

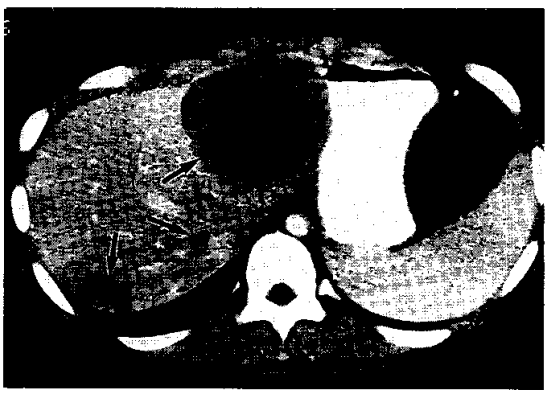

Fig. 2. Two well demarcated mixed density masses were seen in the left lobe and posterior segment of right lobe of the liver. These intrahepatic masses measured 7.0×6.0cm and 2.0×2.0cm in cross, respectively

CLINICAL HISTORY

This 14 years old Korean girl was transferred to the emergency room of Chung-Ang Gil Hospital from a local clinic for the evaluation and management of huge abdominal mass detected by sonogram on December 7, 1991. She had been relatively well until three days before this local visit when she had suffered from suddenly developed and persistent abdominal pain and generalized abdominal distension. Watery diarrhea without nausea and vomiting developed two times per day for last two days. At the time of admission, she showed ill-looking appearance and alert mentality. Blood pressure was 100/70mmHg. Body temperature was 40℃, pulse rate 138 per min., and respiratory rate 20 per min. The conjunctiva was not anemic and the sclera was not icteric. Breathing sound was smooth without rale and heart rate was regular without murmur. Palpable solid abdominal mass was noted with tenderness especially in the right half of abdomen. The mass was not movable. The liver and spleen were not palpable. Laboratory data revealed that hemoglobin was 11.70 gm/dl, hematocrit 38.20%, WBC 13,150/mm^3, platelet 167,000/mm^3. Count was normal. Blood chemistry was within normal limits. Blood urea nitrogen and creatinin were 8 and 0.7mg/dl, respectively. Calcium and phosphate were 10.7 and 4.1mg/dl, respectively. Na and K were 137 and 3.8mEq/L, respectively. Hepatititis surface antigen and antibody were negative and positive, respectively. Alpha-fetoprotein and carcinoembryonic antigen were 6.98 and 1.72ng/ml, respectively. Urine analysis was normal. Simple abdomen revealed a huge abdominal mass and localized ileus.

Abdominopelvic computerized tomogram (Fig. 1-3) revealed that a huge mixed dinsity mass in the abdominal cavity, which was not separable from the pancreas. The mass displaced stomach to the anterior right side. Superiorly, the mass extended to the fundus of stomach, and inferiorly, to the entire mesenteric area, In the pelvic cavity there was mixed density huge mass with ascites. Two well demarcated mixed density masses were seen in the left lobe and posterior segment

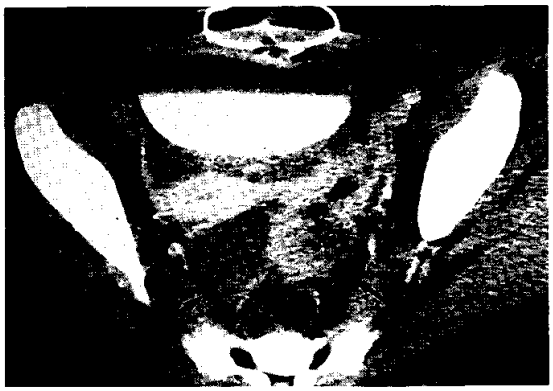

Fig. 3. In the pelvic cavity there was mixed density huge mass with ascites

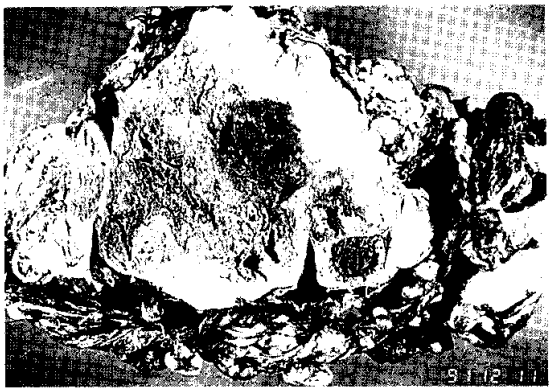

Fig. 5. The cut surface showed creamy white homogenous appearance with multifocal hemorrhages and necrosis (H&E stain)

Fig. 4. Whole mesentery and omentum are involved by huge mass with numerous satellite nodules

of right lobe of the liver. Magnetic resonance imaging revealed low signal intensity in T1 weighted image and high signal intensity with central accentuated high signal intensity in T2 weighted image. Gadolium enhanced T1 weighted image revealed generalized enhancement except central portion

Operative findings showed large amount of turbid ascites with foul odor and a huge conglomerated masses with many satellite nodules in whole omentum and mesentery mimiking metastatic nodules. The tumor measured 30×25×15cm in total dimension. The tumor reached to the transverse colon. The tumor was mainly solid with multifocal hemorrhage and necrosis with calcification. Other retroperitoneal and pelvic organs including kidneys, adrenals, uterus and both adnexae were grossly free. Patial excision of omental tumor and a segmental resection of transverse colon were done.

PATHOLOGIC FINDINGS

The whole mesentery and omentum showed huge firm creamy white mass with many satellite nodules (Fig. 4). On section, the cut surface showed white gray homogeneous appearance with multifocal hemorrhages and necrosis (Fig. 5). The specimen was huge mesenteric mass, which was initially fixed in 10% fromalin, processed routinely and embedded in paraffin. Hematoxylin & eosin, Masson trichrome, periodic acid schiff stain were done. For immunohistochemical study, tissue sections were stained by the DAKO LSAB kit using microprobe (Biomeda). CK22 (DAKO), epithelial membrane antigen, (DAKO), CAM 5.2 (DAKO), vimentin (DAKO), desmin (DAKO), myoglobulin (DAKO), neuron specific enolase (DAKO), S100 protein (DAKO) and glial fibrillary acidic protein (DAKO) were

Fig. 6. Microscopically, the tumor exhibited small nests or solid sheets without organoid pattern separated by myxoid desmoplastic stroma (H&E stain)

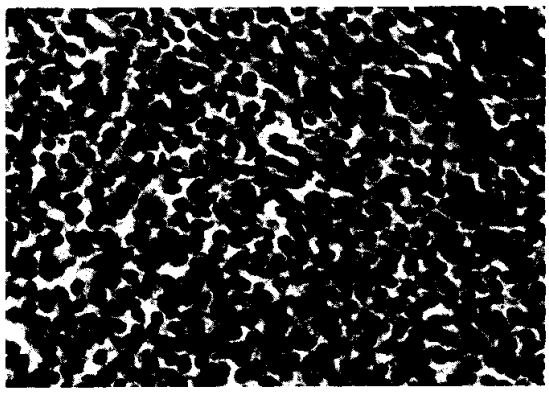

Fig. 7. The neoplastic cells show small size and high N/C ratio. The nuclei are hyperchromatic with inconspicuous nucleoli. The scanty cytoplasm were eosinophilic and their cell borders were indistinct. Mitotic figures were frequent (H&E stain)

used. Appropriate controls were incorporated in all cases, such as colonic epithelium for epithelial marker, vessels for vimentin, colonic smooth muscle for desmin and myoglobulin, peripheral nerve bundles for NSE and S100-protein.

For electron microscopic study, we used initially formalin fixed specimen and refixed in 2.5% glutaraldehyde solution. This specimen was washed in cold 0.1 mol/L phosphate buffer (pH 7.4) alone and put into 1% osmium tetroxide, buffered with 0.1 mol/L phosphate and embedded in eposy resin. Sections were cut with ultramicrotome (Leichert ultramicrotome) stained with uranyl acetate-lead cytrate, and examined under a transmission electron microscope (Hitachi 7100).

Fig. 8. The tumor extends through the colonic wall into the mucosa (H&E stain)

Light microscopic findings

The tumor exhibited solid sheets, and small nests without organoid pattern separated by dense or myxoid desmoplastic stroma (Fig. 6). The neoplastic cells showed small size and high nuclear cytoplasmic ratio (Fig. 7). The nuclei are hyperchromatic with inconspicuous nucleoli. The scanty cytoplasm was eosinophilic and cell borders were indistinct. Mitotic figures were numerous. Individual cell necrosis or confluent necrosis were seen. The tumor extended through the colonic wall to the mucosa (Fig. 8).

Immunohistochemically, the neoplastic cells expressed vimentin (Fig. 9), strongly and diffusely (About 100%) and neuron specific enolase (Fig. 10), stronly and focally (About 30%). However, the neoplastic cells did not expressed cytokerain (CK22), CAM 5.2, epithelial membrane antigen, glial fibrillary acidic proterin, myoglobin, desmin and S-100 protein.

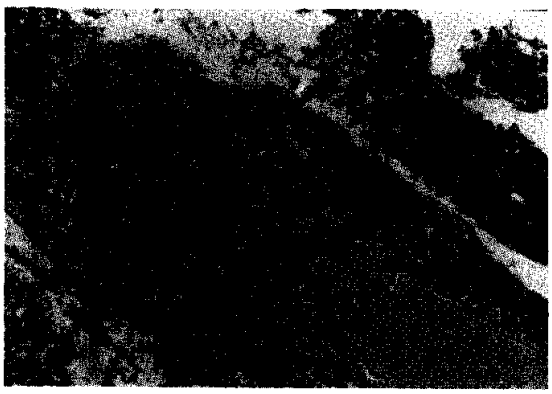

Fig. 9. Immunohistochemically, the neoplastic cells-cytoplasm strongly express vimentin (peroxidase antiperoxidase stain)

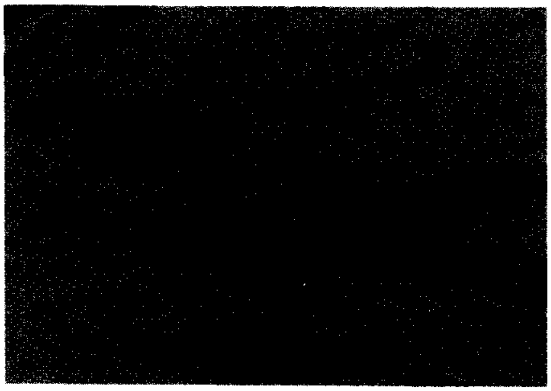

Fig. 10. Immunohistochemically, the neoplastic cells-nuclei and cytoplasm strongly express neuron specific enolase (peroxidase antiperoxidase stain)

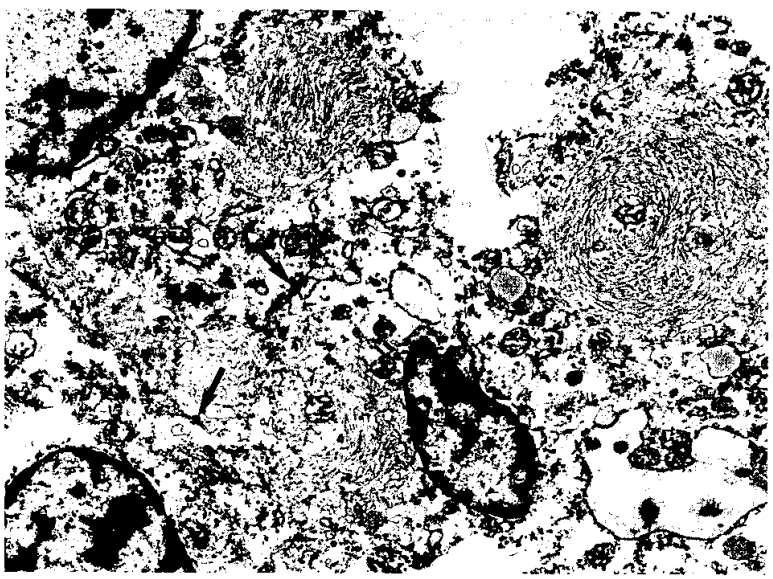

Fig. 11. The nuclear chromatin was coarsely granular heterochromatic. Every tumor cell-cyroplasm contains whorled intermediate filaments in perinuclear portion with entraped organelles. Cytoplasmic membrane is poorly preserved due to formalin fixation, however zonular adherens type juctions (arrows) are seen (×11,500)

Ultrastructural findings

The tumor cells had eccentrically located irregular shaped nucleus and moderate amount of cytoplasm. The nuclear chromatin was coarsely granular and a prominent nucleolus was often seen. The cytoplasm contained whorled intermediate filaments in perinuclear location, resting in nuclear indentation (Fig. 11). Entrapment of several organelles such as round mitochondria, short tubular or dilated rough endoplasmic reticulum, ribosomes and several fat vacuoles were noted (Fig. 12). There was zonula adherens-type intercellular juctions but no definite neurosecretory granules.

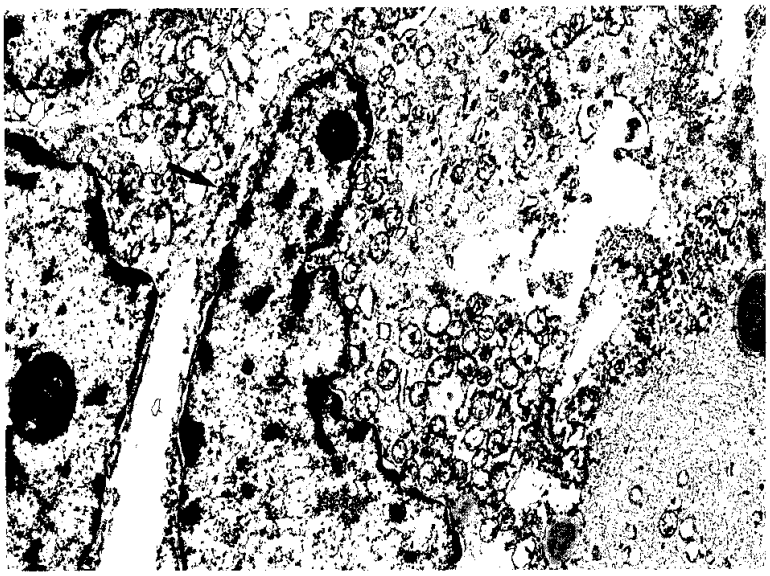

Fig. 12. The nucleus is indented by whorled cytoplasmic intermediate filaments. The other organelles are a fair number of round shaped mitochondria, short tubular rough endoplasmic reticulum, and a few fat vacuoles. Remnant of cytoplasmic membrane with zonular adhrens type junction (arrows) is noted (×13,800)

DISCUSSION

Since Rosai first had called attention to a unique primary peritoneal tumor of childhood in 1988, the characteristic clinicopatologic features of "intraabdominal desmoplastic small cell tumors with divergent differentition" has been established. (Gerald & Rosai; 1989, Ordonez et al.; 1989, Gonzalez-Crussi et al.; 1990, Gerald et al.; 1991) According to analysis of 19 cases by Gerald et al. (1991), the age at the time of diagnosis ranged from 8 to 38 years (mean 18.6 years); all but two of the patients were 30 years or younger. There was a marked male predominance in their group (M:F ratio>5:1). As in our case, the usual symptoms were abdominal pain and distension. The abdominal mass could be palpable in most instances, sometimes in association with ascites. On laparotomy, usually large intra-abdominal mass was associated with numerous smaller peritoneal implants of similar appearance. Microscopically, they were characterized by well defined nests and infiltrating strands of tumor cells separated by cellular or fibromyxoid desmoplastic stroma. The tumor cells were small, with round to oval hyperchromatic nuclei and inconspicuous nucleoli and scant to moderate pale staining cytoplasm. Glandular differentiation was found in several cases (Gerald et al.; 1991). Foci of squamous, or any other recognizable form of differentiation were invariably absent. Central necrosis was common, paticularly in the larger islands. Mitoses were frequent. Lymph node metastases were documented microscopically in one case. Immunohistochemically, the tumor cells exhibited positivity for epithelial marker of keratin and epithelial membrane antigen and mesenchymal marker of vimentin. In addition, many tumor cells showed positive staining for desmin, neuron specific enolase and S-100 protein and were negative for leukocyte common antigen and chromogranin. This is a very unusual combination of multi-immunophenotypic differentiation.

Ultrastructurally, most striking feature of the tumor cells was haphazardly arranged or whorled cytoplasmic intermediate filaments with entraped organelles (Gonzalez-Cruzi et al.; 1990, Gelald et al.; 1991). Cytoplasm contained a fair number of mitochondria, cisternae of rough endoplasmic reticulum, polyribosomes and a few fat vacuoles. The tumor cells contained only rudimentary cell processes and consistently lacked well developed microvilli. Cell junctions were usually scanty,

rather primitive and of the zonula adherens type. A discontinuous basal lamina was identified around the tumor nests in several cases.

In our case, gross and microscopic and ultrastructural features were identical to the previously reported cases but immunohistochemical study did not concur with them. Immunohistochemically, while neoplastic cells of our case expressed diffuse (more than 90% of tumor cells) and strong cytoplasmic positivity for vimentin and focal (about 30% of tumor cells) and strong cytoplasmic and nuclear positivity for NSE, negative for epithelial markers of CAM 5.2, CK22 (pancytokeratin) and EMA. However, distinct clinicopathologic features and ultrastructural features provide undoubted evidence that this tumor is compatible with intraabdominal desmoplastic small cell tumor with divergent differentiation. Ultrastructurally, there was no evidence of any specific carcinoma, lymphoma, neuroblastoma or other neuroepithelial tumor, Ewing's sarcoma, rhabdomyosarcoma or germ cell tumor (Ushigome et al., 1989; Yunis et al., 1979; Triche et al., 1986)

The differenial diagnosis to be considered for this malignant intraabdominal tumor includes malignant lymphoma, mesothelioma, germ cell tumor, rhabdoid tumor and so-called small round cell tumor such as Ewing's sarcoma, embryonal rhabdomyosarcoma, and neuroepithelioma (Dickman & Triche, 1986; Donner et al., 1985 ; Jugens et al., 1988). Based on combination of topographic, morphologic, immunohistochemical, and ultrastructural features, this intraabdominal desmoplastic small round cell tumors did not fit into any of these categories.

The behavior of this tumor proved extremely aggressive (Gerald and Rosai; 1989, Gerald et al ; 1991). The standard treatment was surgical debulking followed by multidrug chemotherapy, sometimes supplemented with irradiation. Typically, an initial response to chmotherapy was followed by uncontrollable tumor relapse. Even in the advanced stages, the bulk of the neoplasm tended to remain within the peritoneal cavity; however, in several instances, this was associated with extra-abdominal metastases.

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