

Mixed Germ Cell–Sex Cord–Stromal Tumor of Non–Gonadoblastoma Type of Ovary – A Case Report –

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We described a case of mixed germ cell-sex cord-stromal tumor of non-gonadoblastoma type (GCST-NG) of the ovary in a 2-year-old girl and compared its histological, immunohistochemical and ultrastructural findings with those of gonadoblastoma. The germ cell component showed an immunopositivity for cytokeratin and epithelial membrane antigen (EMA), and a negative reaction for α -inhibin, alpha-fetoprotein (AFP), placental alkaline phosphatase (PLAP), vimentin and CD99. The sex cord elements showed an immunopositivity for cytokeratin, EMA, vimentin and inhibin, but negativity for AFP, PLAP, and CD99. The ultrastructural features showed desmosome-like cell junctions, suggesting spermatocytic differentiation from the primordial germ cells or gonocytes. Immunohistochemical and ultrastructural findings suggested that GCST-NG is probably a more differentiated form of mixed germ cell-sex cord-stromal tumor than gonadoblastoma.

Key Words : Ovarian Neoplasms–Sex Cord–Stromal Tumor

Mixed germ cell-sex cord-stromal tumors can be divided into two categories: gonadoblastoma and unclassified or non-gonadoblastoma type (GCST-NG). The former is a well recognized tumor that occurs almost exclusively in a patient with abnormal gonadal development and a karyotype containing Y-chromosome material. However, the latter usually occurs in infants or girls under the age of 10 years with normal gonadal development and a normal karyotype.¹ The histopathological characteristics and the clinical behavior of the GCST-NG are not well recognized by the pathologists because of the rarity of documented cases, and it has not yet been described in Korea. Herein, we describe the clinical, histopathological, immunohistological and electron-microscopic findings of a case of GCST-NG that occurred in a 2-year-old girl and compared the findings with those of gonadoblastoma.

CASE REPORT

A 2-year-old girl with an incidentally palpated lower abdominal mass was presented. She had been healthy previously, and showed normal growth and development. The family history was unremarkable. Physical examination of the entire body including the external genitalia revealed no abnormal findings, and there were no clinical symptoms suggesting hormonal abnormality. The serum β -human chorionic gonadotropin (β -hCG) and α -fetoprotein (AFP) levels were within normal ranges, measuring 1.6 ng/mL (normal; 0-20 ng/mL) and less than 3.0 mLU/mL (normal; 0-3 mLU/mL), respectively. Abdominal sonography revealed a solid left ovarian mass.

Upon surgery, the right ovary and other genital organs were unremarkable. Left salpingo-oophorectomy was performed under the impression of dysgerminoma. The left ovary measured 8.5 × 6.5 × 6 cm and weighed 158 g. The external surface was



Fig. 1. The cut surface of the tumor consists of yellowish tan colored area and brownish red colored area.

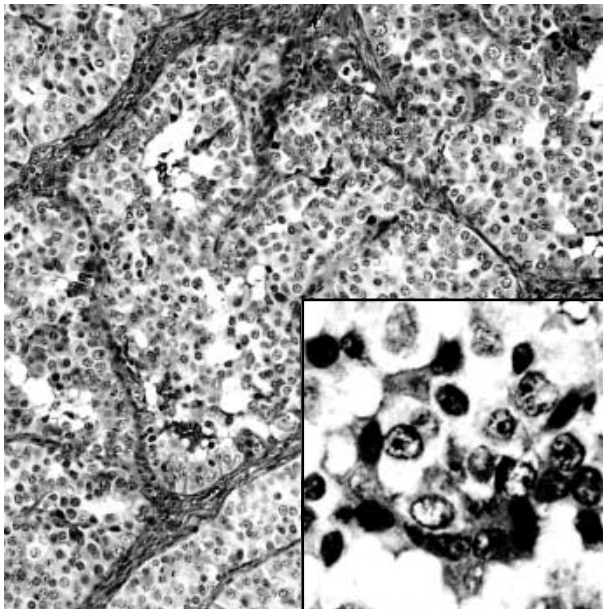


Fig. 2. Histologically, the tumor cells are composed of variable sized, solid or fenestrated tubules with empty lumen or eosinophilic secretory materials in a dense fibrous stroma.

smooth and the cut surface was almost entirely replaced by a well-circumscribed, solid, pinkish tan to yellowish tan, finely trabeculated tissue (Fig. 1). Neither necrosis nor hemorrhaging was present. Histologically, the tumor formed a well-demarcated but unencapsulated mass and was composed of variable sized, solid or fenestrated cell nests and tubules in a dense fibrous

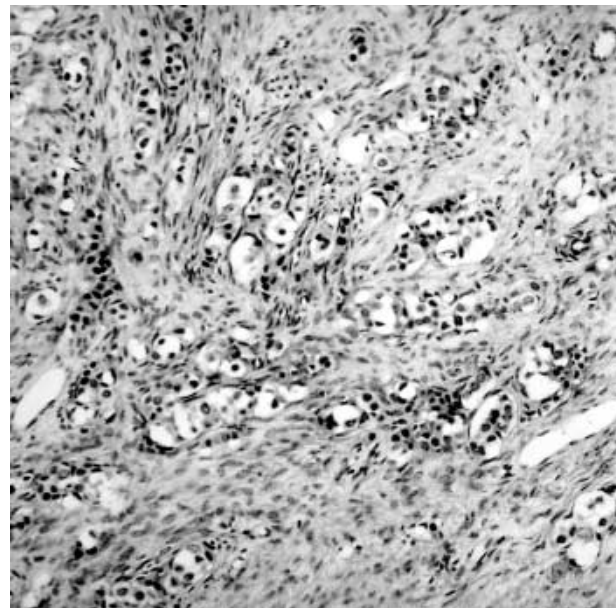


Fig. 3. Both germ cell and sex cord-stromal elements are intimately admixed in the same nests. The tumor cells growing in a long, anastomosing cords and trabeculae is identified.

stroma surrounded by a basement membrane (Fig. 2). The lumen of the tubules was either empty or filled with eosinophilic secretory materials with scalloped peripheral margins; however they did not form the distinctive patterns of gonadoblastoma, such as a hyaline deposit containing eosinophilic basement membrane material or calcification. Infiltrative growth of the tumor cells was identified at the periphery of the tumor, which was composed of both germ cell and stromal elements (Fig. 3). Two different types of cells were intimately admixed in the same nests. One type was the larger cells with round to ovoid nuclei, finely dispersed nuclear chromatin, one or two prominent nucleoli, and abundant pale cytoplasm. The other type was smaller with ovoid or short spindle-shaped, hyperchromatic nuclei, and scanty amount of cytoplasm (Fig. 3). Brisk mitotic figures were present in both cell components. In the normal ovarian tissue on the surface, there were a few normal appearing primordial follicles containing primary oocytes.

The immunohistochemical stainings showed diffuse dot-like positivity for cytokeratin (AE1/AE3; 1:200, Zymed, San Francisco, U.S.A.) in the cytoplasm of the germ cell component (Fig. 4), and weak positivity for epithelial membrane antigen (EMA; 1:200, DAKO, Copenhagen, Denmark), but negativity for α -fetoprotein (AFP; 1:200, Novocastra, U.S.A.), vimentin (1:200, Zymed, San Francisco, U.S.A.), placental alkaline phosphatase (PLAP; 1:200, DAKO, Copenhagen, Denmark), CD99 (1:50, DAKO, Copenhagen, Denmark), α -inhibin

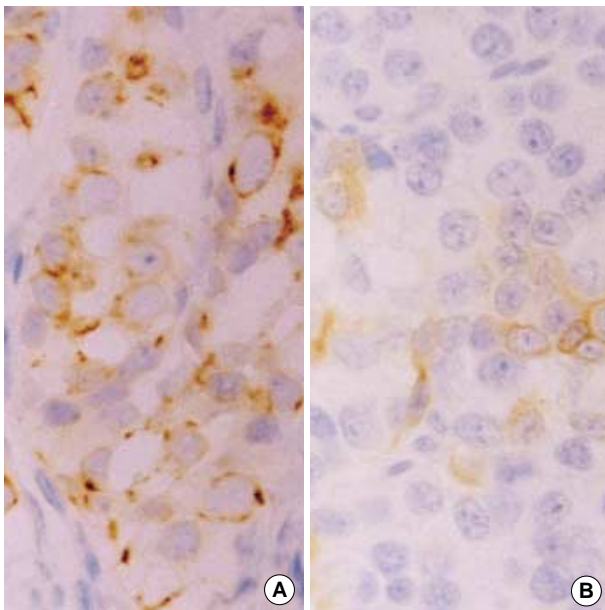


Fig. 4. (A) Immunohistochemically, both germ cell and stromal elements show focal dot-like positivity for cytokeratin. (B) The stromal element shows focal positive reaction for α -inhibin.

(1:50, Serotec, Oxford, U.K.) and carcinoembryonic antigen (1:100, DAKO, Copenhagen, Denmark). The stromal element showed weak immunopositivity for cytokeratin, EMA, α -inhibin, and vimentin, but negativity for PLAP, CD99, and AFP.

On electron-microscopic examination, the tumor cell nests were surrounded by basal lamina. Primitive desmosome-like cell junctions, which are frequently identified along the spermatocytic differentiation, were focally identified. The tumor cells had prominent nucleolemma, heterochromatic nuclei, abundant ribosomes, and mitochondria (Fig. 5). Sex cord elements did not contain annulate lamellae or Charcot-Böttcher crystals.

A chromosomal study was not performed. After the left salpingo-oophorectomy, no other adjuvant therapy followed, however, the patient is doing well without evidence of tumor recurrence or metastasis during 8 months of postoperative follow-up.

DISCUSSION

GCSCT-NG differing from gonadoblastoma was described by Talerman in 1972.² It considered to be distinctive clinically and pathologically.³ The tumor is very rare and there was no reported case in Korea. Most cases are found in infants and children younger than 10 years, but rare cases occur in adults.⁴

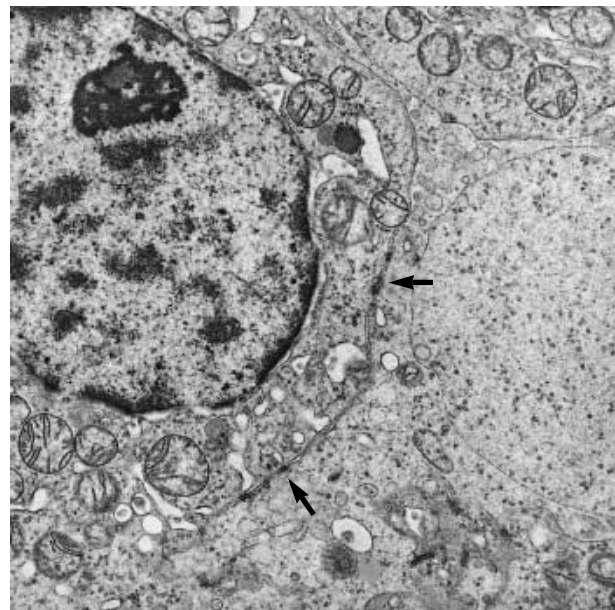


Fig. 5. Electron-microscopic findings. The larger tumor cells are surrounded by basal lamina and have focal desmosome-like primitive cell junctions (arrows). The cytoplasm contains abundant ribosomes and mitochondria ($\times 8,000$).

The patients with this tumors have been considered to have a benign clinical course without the emergence of a coexisting malignant germ cell tumors.² However, recently, a recurrent case of GCSCT-NG showed multiple tumor implants on the abdominal wall and peritoneum and, in another case, a mixed tumor of a gonadoblastoma and a GCSCT-NG has been described.^{4,5} Therefore, histogenesis and the relationship between the gonadoblastoma need to be further studied. Comparing to gonadoblastoma, the tumor occurs as a unilateral ovarian or testicular mass in the phenotypically and karyotypically normal females or males.^{1-4,6,7} The tumor is usually lacking typical features of gonadoblastoma such as Call-Exner-like bodies, calcification and hyalinization.^{2-4,7}

A variety of diseases should be considered in the differential diagnosis in this case. The possibility of gonadoblastoma was considered because of the two cell components in the tumor cell nests. However, the characteristic histologic findings, such as hyaline deposit or calcification, as well as typical clinical features of gonadoblastoma were not identified. Yolk sac tumor should also be excluded at the age of this patient because it may have various histologic patterns. However, the absence of typical histologic features of yolk sac tumor, immunonegativity for AFP and the normal range of serum AFP level were helpful to exclude a yolk sac tumor. Juvenile granulosa cell tumor was also considered because of tubular or macrofollicular patterns with secretory materials, however, immunohistochemical stain-

ings for α -inhibin and CD99, which are well-known immunohistochemical markers of the ovarian sex-cord stromal tumors, showed only weak positivity in the intervening smaller stromal element, but not in the larger tumor cell component. Dysgerminoma, in which tumor cells may occasionally form irregular or rounded gland-like spaces or solid tubular structures, was another possibility. However, the presence of two different cell components, absence of lymphocytes, diffuse immunopositivity for cytokeratin and EMA and the immunonegativity for PLAP in the larger tumor cell component were helpful to exclude the diagnosis of dysgerminoma. Histologic features of the larger cell component in this tumor resemble dysgerminoma or germ cell components of the gonadoblastoma, however, immunopositivity for cytokeratin, negativity for PLAP and desmosome-like intercellular junctions suggested cytologic differentiation toward spermatocytes from primordial germ cells.² Immunohistochemical staining for PLAP is usually positive in the dysgerminoma, gonadoblastoma or other germ cell tumors and in the normal primordial germ cells of the fetal ovary,⁸ but is negative in the primary oocytes within the primordial follicles. Therefore, immunohistochemical and electron-microscopic findings suggested that GCSCT-NG might be a further differentiated tumor compared to gonadoblastoma.

In conclusion, GCSCT-NG is very rare tumor, but it should always be considered in the differential diagnosis of ovarian and testicular tumors in children. A correct diagnosis is crucial for treatment of children with these tumors.

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