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CASE REPORT/OLGU SUNUMU

An 11-year-old girl with juvenile-type granulosa cell tumor of the ovary that recurs in a short time: a case report

Kısa sürede nükseden overin juvenil tip granüloza hücreli tümörü olan 11 yaşında kız hasta: olgu sunumu

Oğuz Arslan[1], Burak Giray[2], Emir Erhan Dönmez[2], Doğan Vatansever[2], Çağata Taşkıran[2]

[1] University of Health Sciences Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital, Department of Obstetrics and Gynecology, Istanbul, Türkiye
[2] Koc University School of Medicine, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, Istanbul, Türkiye

ABSTRACT

Aim: Ovarian tumors with granulosa cells constitute 2-5% of all malignant ovarian tumors. Its incidence among sex cord stromal tumors is over 90%. There are two subtypes of granulosa cell tumors; adult type (95%) and juvenile type (5%). In this study, we aimed to show the recurrence of juvenile granulosa cell tumors.

Case presentation: We presented a case with a diagnosis of juvenile granulosa cell tumor of the ovary, which was diagnosed at the age of 11, although it was stage 1A, but relapsed at the postoperative 14th month and underwent cytoreductive surgery.

Conclusion: Although juvenile granulosa cell tumor of the prognosis is good in the early stages; it is important to follow up closely due to the risk of recurrence.

Keywords: Juvenile granulosa cell tumor, Ovary, Puberty

ÖZET

Amaç: Granüloza hücreli over tümörleri tüm malign over tümörlerinin %2-5'ini oluşturur. Seks kord stromal tümörleri arasında görülme sıklığı %90'ın üzerindedir. Granüloza hücreli tümörlerin iki alt tipi vardır; yetişkin tipi (%95) ve juvenil tipi (%5). Bu çalışmada juvenil granüloza hücreli tümörlerin nüksünü göstermeyi amaçladık.

Olgu sunumu: Overin juvenil granüloza hücreli tümörü tanısıyla 11 yaşında evre 1A olmasına rağmen tanısı konulan, postoperatif 14. ayda nüks eden ve sitoredüktif cerrahi yapılan bir olguyu sunduk.

Sonuç: Juvenil granüloza hücreli tümörün erken dönemde prognozu iyi olmakla birlikte; tekrarlama riski nedeniyle yakın takip önemlidir.

Anahtar Kelimler: Juvenil granüloza hücreli tümör, Yumurtalık, Ergenlik

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Correspondence: Oğuz Arslan,University of Health Sciences Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital, Department of Obstetrics and Gynecology, Istanbul, Türkiye. E-mail: oguzarslan29@hotmail.com

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INTRODUCTION

Granulosa cell tumors develop in the sex cord stroma of the ovary. They are ovarian neoplasms that show signs of virilization and estrogen excess by secreting steroid-derived hormones (1). Ovarian tumors with granulosa cells constitute 2-5% of all malignant ovarian tumors. Its incidence among sex cord-stromal tumors is over 90%. There are two subtypes of granulosa cell tumors; adult type which constitutes 95% of cases, and juvenile type which constitutes 5% of cases. Juvenile granulosa cell tumors (JGCT) are generally seen in premenarchal girls. About 90% of the JGCT cases are in women under 30 years, and the mean age is between 8-13 years (2). In this study, we report a case of JGHT, a rare tumor in an 11-year-old girl.

CASE PRESENTATION

An 11-year-old female patient was admitted to an external medical facility due to menstrual bleeding that had been going on for 1 month. According to the patient's medical history, she began menstruating at the age of 10 and experienced abdominal pain, prompting her to seek care at an external medical facility. Abdominal computed tomography (CT) was performed on the patient and a 4 cm mass was detected in the right ovary. A right salpingo-oophorectomy operation was performed and the mass's histopathology was JGCT, stage 1. After surgery, she received 4 cycles of cisplatin, etoposide and ifosfamide-based chemotherapy. In the follow-up period, amenorrhea occurred 14 months after the operation. During the patient's follow-up, a pelvic ultrasound revealed a mass in the left ovary, and surgery was recommended again. However, the patient declined treatment and presented to our clinic for re-evaluation. Physical examination revealed a distended abdomen, fullness in the pelvic and suprapubic regions, tenderness, and dullness on palpation. Magnetic resonance imaging (MRI) revealed a 10x10x12 cm mass in the left ovary, an 8x5cm metastatic mass in the subdiaphragmatic area that caused external pressure on the liver from the right lateral, subdiaphragmatic peritoneal implants, lymph nodes of 10x5 mm, and diffuse ascites. Inhibin B level was 243 (2-80) pg/mL and CA 125 level was 98 (0-35) U/ml. Tru-cut biopsy was performed with USG guidance for the peritoneal implants. The final result of histopathological examination was JGCT. No metastasis was detected in the thorax CT. Recurrence was detected 14 months after the primary surgery, and secondary cytoreductive surgery was planned. Intraoperative frozen section examination revealed tumor infiltration on the uterus and rectum but no metastases were observed in the right pleura, lymph nodes at the level of right iliac bifurcation and the left external iliac artery. Abdominal hysterectomy, left salpingo-oophorectomy, cytological sampling, pelvic (3 lymph node) paraaortic (14 lymph node) lymph node sampling, omentectomy, appendectomy, diaphragm stripping, low anterior resection and colorectal anastomosis were performed. In the histopathological examination of the mass in the left ovary, the tumor diameter was 10 cm, the tumor shows solid development in most areas, and capsule invasion is observed. The mitosis rate was 20 in 10 magnification areas. Poorly differentiated tumoral infiltrates, which consist of cells with narrow cytoplasm and mostly from pseudo-papilla-like structures, were observed. Cells suspicious of malignancy were detected in cytological sampling. Tumoral infiltrates were detected in the omentum, Morrison pouch, liver capsule, small intestine, right diaphragm peritoneum, and sigmoid mesocolon. No metastases were observed in the

liver parenchyma, uterus, appendix, left ovarian vein, ileum meso, over the cecum, low anterior resection, ligamentum teres, and right pleura. No metastases were observed in the lymph nodes in the pelvic, left paraaortic, precaval, supra-porta and inter-aortocaval areas. After the immunohistochemical examination, tumor cells showed positive reaction with CD56, EMA, inhibin, calretinin, SF1. No staining was observed with Glipican-3, PAX8, WT1. SALL4, which has been applied for the differential diagnosis of germ cell tumor. No loss of nuclear expression was detected in tumor cells with SMARCA4, which was applied for hypercalcemic type small cell carcinoma of the ovary. According to these results, the Stage was IIIC. The patient received 6 cycles of chemotherapy (carboplatin paclitaxel) and maintain bevacizumab therapy. After 4 months from secondary cytoreductive surgery, brid ileus occurred and she underwent laparotomy. Seven months after secondary cytoreductive surgery, an 8 cm suspicious intra-abdominal cystic mass was identified in the right upper quadrant adjacent to the liver on abdominal CT, and the patient subsequently underwent laparotomy. In the histopathological examination of the materials taken, lymphocele, necrotic granuloma, and microabscess foci were detected, but no recurrence. She has been followed for 19 months after secondary cytoreductive surgery, and no evidence of clinical recurrence or metastasis has yet been detected.

DISCUSSION

The mean age of occurrence of JGCTs is 13, and 78% of patients are younger than 20 years of age. Patients apply to the clinic with isosexual pseudo praecox in the premenarchal period and apply to the clinic with complaints of abdominal pain, distention, amenorrhea, and menstrual irregularity in the adolescence period (3). In this case report, the patient's complaint at admission was menstrual irregularity and abdominal pain. Serum inhibin levels may be elevated in JGHTs. Inhibin is secreted from ovarian granulosa cells and suppresses follicular stimulating hormone (FSH) levels with a negative feedback effect. It can cause amenorrhea. Elevated inhibin levels are not specific (4). In our case, serum inhibin levels were also increased. Malignancy should be considered in recurrent ovarian cysts, in cysts that do not regress in 3-month follow-up, and in cysts with solid components. JGHTs can be solid, solid-cystic, or completely cystic with an average size of 12.5 cm. There is a 4x3cm solid component in a 10x10x12 cm cyst detected in the left ovary of this patient. Irregular follicles and pleomorphic nuclei are seen in the histopathological examination of JGHTs. Nuclear grooves and Call-Exner bodies are usually not observed (5). In the pathological examination of our case, poorly differentiated cells consisting of cells with narrow cytoplasm and mostly forming pseudo-papilla-like structures are observed. In immunohistochemical studies of JGHTs, the tumor typically shows a positive reaction with inhibin or calretinin. The histopathology of our patient's tumor showed a positive reaction to both inhibin and calretinin. High mitotic activity (≥20 per 10 high power fields) was observed in the tumor.

The prognosis for JGHT is generally well. Although it is less differentiated than the adult type, its cure rate is higher. Stage is the most important prognostic factor. They are usually diagnosed at an early stage and show a good course. However, they are more aggressive in FIGO stage II, III, or IV patients. Treatment of JGCTs is usually unilateral salphingoopherectomy. Surgery is sufficient in

stage 1A patients. Adjuvant chemotherapy is recommended for patients with stage 1C and more (6). In children with advanced juvenile granulosa cell tumors, adjuvant chemotherapy appears to contribute to long-term complete remission and is generally recommended for those with stage IC disease and a high mitotic index (≥20 per 10 high power fields). Our patient was stage 3C recurrence and metastasis and cytoreductive surgery was performed. The patient experienced recurrence 14 months after the primary surgery. An interim report from the 2020 annual meeting of the American Society of Clinical Oncology indicated that the median time to recurrence for patients with juvenile granulosa cell tumors was 11.5 months (range 3-19) (7). Then, our patient received adjuvant chemotherapy with carboplatin and paclitaxel. Bevacizumab was given to our patient as an antiangiogenic treatment. Chemotherapeutic options may include retreatment with a platinum-based regimen. The value of taxanes has been reported, especially in combination with platinum agents. Although data are limited, angiogenesis inhibitors appear to be promising in the treatment of JGHTs (8).

In conclusion, we presented a patient with an early-stage juvenile granulosa cell tumor that relapsed in a short time. Although the prognosis is good in the early stages, it is important to follow up closely due to the risk of recurrence.

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