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Case report

Ovarian sex cord stromal tumor with annular tubules in a 7-year-old child: A case report

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ABSTRACT

A seven-year-old girl who presented with precocious puberty was diagnosed with an estrogen-secreting right ovarian tumor. Right salpingo-oophorectomy with staging was performed by gynecologic oncologists. Intraoperative frozen section reported sex cord stromal tumor. Histopathological report confirmed sex cord stromal tumor with annular tubules with brisk mitotic counts (17 per 10 high-power fields). The post-operative course was uneventful. She remained asymptomatic with normalisation of serum estradiol upon six-month follow-up.

1. Introduction

Sex cord stromal tumor with annular tubules (SCTAT) represents a rare type (2.3%) of sex cord stromal ovarian tumor (SCST) (Qian et al., 2015). It is distinguished by its ring-shaped tubules. It has morphological features between Sertoli cell tumor and granulosa cell tumor.

There are two subtypes of SCTAT, Peutz-Jeghers syndrome (PJS)-related and sporadic. PJS-related SCTAT constitutes 36% of all SCTAT (Young et al., 1982). While most PJS-related SCTAT is benign, 20% of the sporadic subtype is malignant. Most women present at second and third decades of life with symptoms of hyperestrogenism. Although unilateral salpingo-oophorectomy is curative, recurrence is an important issue. Given its rarity, there is no standardized management algorithm worldwide.

Currently, there is sparse literature on SCTAT in pediatric population (Sohl et al., 1983). We reported a case of sporadic SCTAT in the rare pediatric age group with an even rarer microscopic finding of high mitotic count.

2. Case presentation

A Chinese girl with good past health was referred by the Student Health Service for premature breast development at 6.5 years old and vaginal spotting since seven years old. She had no axillary, pubic hair growth or rapid increase in height. She had no headache, abdominal pain, visual disturbance, café-au-lait spots or history of hormonal intake.

Physical examination revealed height at 50th percentile for age. She reached Tanner stage three breast development and Tanner stage one pubic hair development. Blood test revealed raised estradiol level to 81 pmol/L (22.1 pg/mL). Luteinizing hormone releasing hormone (LHRH) stimulation test showed suppressed response with all stimulated follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels equal or less than 0.2 iu/L. Serum prolactin and thyroid function were normal. Tumor markers including alpha fetoprotein (AFP), human chorionic gonadotropin (HCG), CA-125 (cancer antigen 125) were not raised. Bone age was 8.7 years at the chronological age of 7.5 years. Both ultrasound and magnetic resonance imaging of pelvis revealed a right heterogenous adnexal mass of 5.6 × 5.3 × 6.8 cm in size.

The patient was assessed by gynecologic oncologists with clinical diagnosis of estrogen-secreting ovarian tumor and peripheral precocious puberty. At staging laparotomy, a 9 cm right ovarian tumor replaced the right ovary. It was smooth and mobile with no tumor breaching the capsule. There was light yellowish straw-colored fluid in the peritoneal cavity. The left ovary, fallopian tubes, uterus and peritoneal lining were normal. Frozen section of the right ovary showed a sex cord stromal tumor. Right salpingo-oophorectomy was performed. Peritoneal washing and diaphragmatic scraping were obtained for cytology. Bilateral paracolic gutters, Pouch of Douglas (POD) and omental biopsy were taken for section and no malignancy was identified. Serum estradiol level was < 37 pmol/L (< 10.1 pg/mL) one day after the operation. She had an uneventful post-operative course and was

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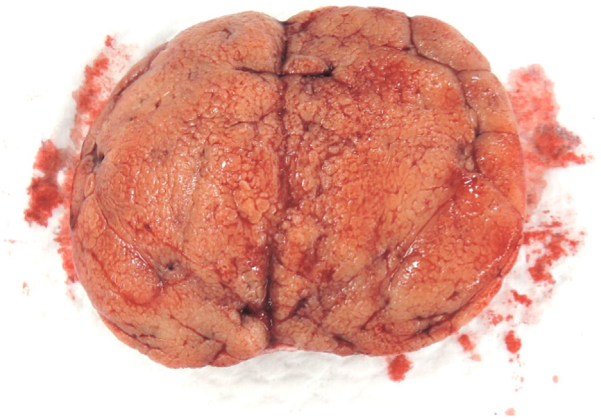

Fig. 1. The cut surface of the ovarian tumor.

discharged three days afterward.

Upon follow-up two months later, the breast size regressed and vaginal bleeding subsided. At the time when the case was reported six months after the operation, ultrasound scan of the pelvis showed no evidence of recurrence. Further examination did not reveal signs of PJS, e.g., melanocytic macules on the lips or signs of gastrointestinal bleeding which might indicate hamartomatous polyps. There was no family history of PJS or gastrointestinal cancer. She is having long-term follow-up by both pediatrician and gynecologic oncologist.

The 9 × 7 × 5 cm right salpingo-oophorectomy specimen was sent for section. The histopathological report was SCTAT. Macroscopically, it was a multilobulated tan-colored tumor (Fig. 1) with a smooth capsule. The fallopian tube was 7 cm long and 0.6 cm in diameter. Two frozen blocks and eight paraffin blocks were processed. Histologically, the paraffin section showed nodular aggregates of complex annular tubules and coalescent nest of tumor cells (Fig. 2A). There were multiple intercommunicating rings around hyaline bodies. The nuclei were round and oval shaped without pleomorphism. The cytoplasm was eosinophilic and foamy. The mitotic counts were high (17 per 10 high-power fields) (Fig. 2B). There was no germ cell component or tumor necrosis. The tumor capsule was not breached. The peritoneal washing and bilateral subdiaphragmatic scrapping were both negative for malignant cells. The tumor was classified as FIGO (the International Federation of Gynecology and Obstetrics) Stage IA. With immunohistochemical staining, the tumor was positive for inhibin, calretinin, MNF 116 and WT1 staining (Fig. 3). Other immunohistochemical markers for placental alkaline phosphatase (PLAP), CD 117, synaptophysin and chromogranin were negative.

3. Discussion

SCTAT has low malignant potential with late recurrence. Being an estrogen-secreting tumor, girls usually present with isosexual precocity while adult women typically present with irregular menstrual bleeding (Ueki et al., 2011). Other presentations include incidental finding of an abdominal mass with or without pain. Although most of the SCTAT are picked up by ultrasound or advanced imaging, the diagnosis is ultimately made by pathological examination.

SCTAT is composed of cells from sex cord derivation aligned as ring shaped tubules. The absence of germ cell component excludes the diagnosis of gonadoblastoma. Being a separate entity from SCST, the distinctive features of SCTAT include antipodal arrangement of the nucleus, the presence of fibrous stroma and eosinophilic hyaline cores within the nests. SCTAT expresses characteristic positive staining for markers (inhibin, calretinin, WT 1, CK) on immunohistochemistry. Nuclear atypia and mitotic figures are otherwise not common features.

The two subtypes of SCTAT differ in terms of the age of onset, initial presentation and its nature. Firstly, sporadic SCTAT generally presents at a later age in life (mean, 34 years for sporadic SCTAT; mean, 27 years for PJS-related SCTAT). Secondly, more patients with sporadic SCTAT present initially with abnormal menstrual bleeding (68.1% vs 40.7%) and abdominal mass (51.1% vs 14.8%) than PJS-related group (Young et al., 1982). Thirdly, sporadic SCTAT, which could be both solid and cystic, is unilateral and more than 3 cm in diameter (Song et al., 2006). It typically has a tan-colored cut surface. Apart from secreting estrogen, a few of the literature reported progesterone secretion. On the contrary, PJS-related SCTAT is bilateral, less than 3 cm in diameter and multifocal (Young et al., 1982). Some also demonstrate calcification. Apart from the above distinctive features, germline mutation of STK11 gene also points towards PJS-related SCTAT.

Based on the tumor characteristics and the absence of PJS features, our patient likely harbored sporadic SCTAT. We did not perform ovarian biopsy as the disruption of the tumor capsule may worsen the prognosis by tumor seeding. The first-line treatment of SCTAT is surgical excision. Fertility conservation is a key issue in young aged girl. We performed a unilateral salpingo-oophorectomy in view of minimal salvageable ovarian tissue. Secondly, high rate of recurrence was reported after pure ovarian cystectomy. As mentioned, salpingo-oophorectomy is deemed curative for unilateral intact tumor (Qian et al., 2015). As for PJS patients, wedge resection or biopsy of the contralateral ovary should be performed due to high rate of bilateral involvement. Up till now, there are no studies comparing the outcome after unilateral or bilateral oophorectomy in PJS patients with bilateral SCTAT. The performance of staging operation in our patient is also well justified given the higher risk of malignancy in sporadic subtype of SCTAT.

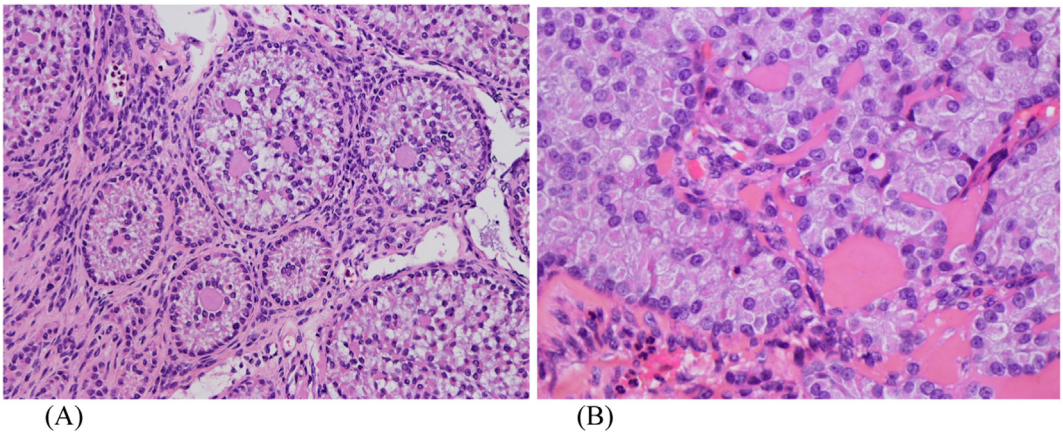

Fig. 2. Hematoxylin and eosin stain of the ovarian tumor. (A) complex annular tubules with hyaline bodies (B) readily identifiable mitosis.

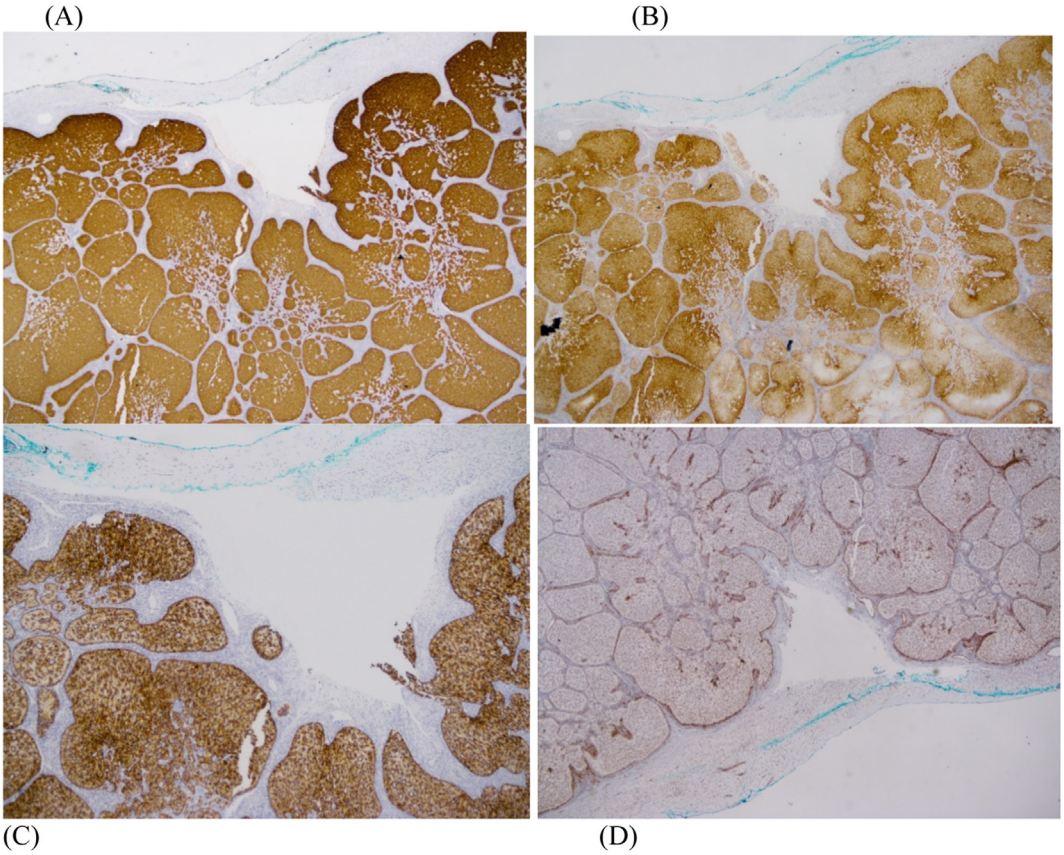

Fig. 3. Positive immunohistochemical staining on the tumor specimen. (A) inhibin staining (positive). (B) calretinin staining (positive). (C) MNF116 staining (positive). (D) WT1 staining (positive).

Recurrence of sporadic SCTAT ranges from 8.5% to 46.2% (Young et al., 1982; Qian et al., 2015). The latency period ranges from three months to 20 years. Although no specific guidance is present from international bodies, most of the authors agreed on long-term follow-up for these patients. Meticulous history taking for menstrual disturbance, physical finding of abdominal mass, blood taking for tumor markers (estradiol and progesterone) and serial imaging should be used for surveillance of recurrence. Most recurrence occurs at the retroperitoneum especially at ipsilateral paraaortic or pelvic lymph node which can be detected by computed tomography and PET (positron emission tomography) scan (Slimane et al., 2016). Differ from epithelial ovarian cancer, surgical excision is still the mainstay treatment at recurrence. Although no treatment algorithm was available, literature suggested total hysterectomy, remaining salpingo-oophorectomy and lymphadenectomy (Slimane et al., 2016). Fertility sparing surgery with recurrent tumor resection (RTR) is also feasible for patients with no involvement of contralateral ovary and uterus. Complete remission had been achieved even after multiple recurrences (Qian et al., 2015).

The role of adjuvant treatment is unclear. There are reports of the use of radiotherapy and chemotherapy for disease control but the role of preventing recurrence is unproven.

SCTAT is rare. Yet, our patient has an even rarer presentation. Firstly, most of the reported SCTAT occurred in women in reproductive age. There were only seven reported prepubertal girls out of 74 patients in a review (Young et al., 1982). Among these seven girls, five of them were sporadic with the youngest age of six. The details of their treatment outcome were not mentioned individually. Nosov et al. reported a five-year-old girl with sporadic SCTAT treated by unilateral salpingo-oophorectomy with staging (Nosov et al., 2009). Secondly, while the reported mitotic count in malignant SCTAT varied from 1 to 10 per 10 high-power fields (Young et al., 1982; Gloor, 1979), the present case which did not reveal features of malignancy had a brisk count of 17 per 10 high-power fields. Despite the fact that its clinical implication was not clear, the rate of recurrence might presumably be increased. Despite the high recurrence rate, the prognosis of SCTAT is favorable. The 1-year and 5-year progression-free survival (PFS) is 92% and 67% respectively. The median PFS time is 97.8 months. The 5-year overall survival rate is 100% (Qian et al., 2015).

4. Conclusion

Long-term follow-up is prudent for patients with SCTAT in view of high recurrence rate. Surgical excision is curative. The role of remaining salpingo-oophorectomy and hysterectomy to patient without fertility wish should be looked into. Further research should investigate the efficacy of lymphadenectomy. Systematic long-term follow-up data would be useful.

5. Ethics approval and consent to participate and consent for publication

Written informed consent was obtained from the patient and parents. It was approved by the Institutional Review Board of Hospital Authority's New Territories West Cluster ethics committee of Hong Kong.

Author contribution

LTK and KYF conceptualized this case report. LTK, LMW and TWSL were in charge of drafting the manuscript. LMW, YFK and HFH were responsible for managing and performing surgery on the patient. TWSL was the in-charge pathologist. YFK, HFH, LMW and TWSL supervise the

whole submission process. All authors were responsible for editing the final manuscript.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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