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A Rare Case of an Ovarian Seromucinous Borderline Tumor in a Young Child

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Abstract:

Objective: *to present a rare case of an ovarian seromucinous borderline tumor in a young child*

Design: *case study*

Setting: *Department of Obstetrics and Gynecology, Fatmawati General Hospital*

Patient: *an ovarian seromucinous borderline tumor in a fourteen year old girl with chief complaint of abdominal enlargement since 5 month before admission*

Results: *Conservative surgery as ovarian cystectomy and salpingooophorectomy is adequate for benign lesions.*

Conclusion: *Postoperatory monitoring of patients plays a critical role in case of any possible relapses, especially consequent malignant evolutions. Accurate diagnosis and clinical staging lead to better treatment results, and reduce the use of unnecessary aggressive therapies.*

Keywords: seromucinous, borderline tumor, conservative surgery

1. INTRODUCTION

Majority tumors of the ovary can be classified into one of three majorcategories; surface epithelial-stromal tumors, sex cord-stromal tumors,and germ cell tumors according to the anatomic structures from whichthe tumors presumably originate.[1]Epithelial cell tumors of the ovaries are derived from malignanttransformation of the epithelium cells of the surface ofthe ovary. These cells come from the primitive mesoderm andare capable of undergoing metaplasia. The six primary typesof epithelial tumors are serous, mucinous, endometrioid, clearcell, Brenner, and undifferentiated (Fig 1).[2]Ovarian epithelial tumours account for approximately two-thirds of all ovarian neoplasms and their malignant forms represent about 90% of ovarian cancers.Epithelial ovarian tumor are majority in adult women, but unusual in a young child. The incidence of malignancies is 1% to 1.5%, and the majority histologic type is non-epithelial type such as germ cell tumors or sex cord-stromal tumors. A small proportion of ovarian tumors in children (approximately 15% - 20%) is derived from the ovarian epithelium.Epithelial ovarian tumor are commonly found in adults, and the mean age at diagnosis of ovarian cancer is 63 years, but these tumors, including serous and mucinous types, are extremely rare in young children.[2, 3]

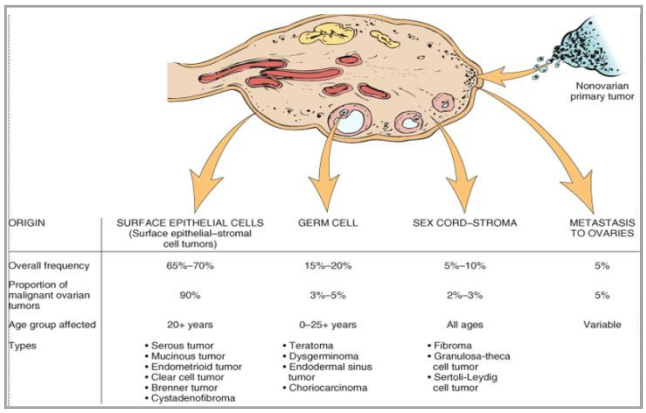

Figure 1. *Classification of various ovarian neoplasms.*

The recent World Health Organization (WHO) 2014 classification of tumors of female reproductive organs introduced a new category of ovarian neoplasm designated as “seromucinous tumors” as they exhibit both serous and mucinous features.[4-6]Seromucinous cyst of the ovary are uncommon occurrence in young children, it is more common in women more than 20 years. Seromucinous borderline tumors (SMBTs) are characterized by complex papillary architecture reminiscent of serous tumors but composed of mucinous epithelium.[7]These seromucinous tumors are composed of serous cells, endocervical type of mucinous epithelium, endometrioid cells, squamous cells and undifferentiated cells.[5]It is important to correctly diagnose these rare tumors in young child in order to assure proper treatment and to prevent mortality and preserve fertility. Only few cases of an ovarian borderline type seromucinous tumor in premenstrual girl have been reported in

literature.Relatively little is known concerning the etiology of seromucinous ovarian cysts, although hormonal factors appear to be important.[8-10]

Here we present a rare case of an ovarian seromucinous borderline tumor in a fourteen year old girl with chief complaint of abdominal enlargement since 5 month before admission.The histological features of borderline tumors, rapid enlargement of the ovarian mass, the young age, make this case interesting for publication.

2. CASE REPORT

We report the case of a fourteen year old girl who presented to our hospital with abdominal enlargement over five months was referred to our hospital for diagnosis and treatment in August 2017. The last menstrual cycle was 5 months prior and she denied the use of any illicit drugs. Her menstrual cycle was regular and she experienced menarche at the age of 12 years. There was no significant family history.There was no reported use of oral contraceptives, and she was not known to be sexually active.There was no complain of nausea, vomitus, vaginal bleeding, urinate and defecation.Physical examination revealeda blood pressure at 110/70 mmHg, respiratory rate 20 breaths/minute, pulse rate 88/minute, temperature of 36.5^{o}C, normal cardiac and respiratory sounds.Her abdominal examination showed enlargement and a firm mass without tenderness, extending from the pelvis to toprocessusxiphoideus. Gynecology examination:inspection: vulva urethra within normal limit, inspeculo : not performed, rectal toucher : Uterus difficult to be evaluated, there was a palpable mass on right & left adnexa until processusxiphoideus, sphincter ani tone was good, ampulla was not collapsed, rectum mucosa was smooth.

Laboratory test revealed normal complete blood count, kidney and liver function test. On tumor marker analysis, CA 125 (63.35 U/mL) was elevated.Gynecologic ultrasonography showed a large cystic mass with solid part, echointernal, multilocular and vascularization RI 0.38with size 30x12 cm according toovarian cystic neoplasm type mucinous (Fig 2).Abdominal contrast-enhanced computed tomography (CT) images of the whole abdomen showed a large multilocular tumor of size approx 11.7 x 21.5 x 28.9 cm with solid part, the tumor compressed the whole intraabdominal organ to the posterior and calcification on pelvic region until abdomensuspected malignant ovarian cystic neoplasm(Fig 3).

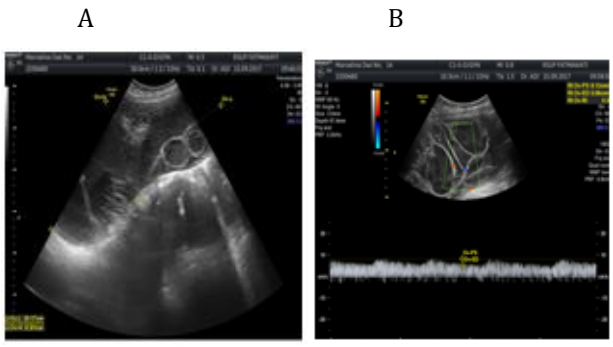

Figure 2. *Ultrasound images. (A) a cystic mass size 30x12 cm. (B) multilocular and vascularization positive*

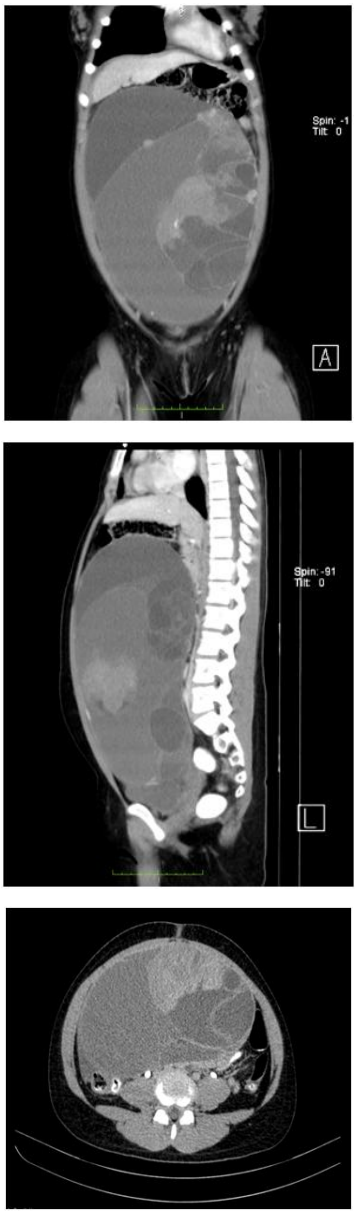

Figure 3. *CT Scan: a largecystic mass, multilocular tumor with clear boundaries spreading throughout the whole abdominal cavity from the pelvis into the upper abdomen.A. Coronal & Sagital view B. Axial view*

The patient underwent laparotomy with a midline incision. Intraoperatively, a large mass measured 30 x 20 x 13 cm was found to originate from the left adnexa,independent of surrounding organs and with no adhesion to the small intestine or colon(Fig 4).The right adnexa, uterus, liver, peritoneal was grossly normal. The left ovarian tumor had a smooth external surface but showed increased vascularity on the tumor surface. It was removed directly from the abdominal cavity, because the appearance of a benign cyst and a girl was still 14 years old, a left salpingooophorectomy was performedbecause the masswas adherent to the left ovary and the left fallopian tube was unhealthy. Theuterus and right adnexa were left intact as there was no apparent infiltrationor any other signs of metastasis. the surgical specimen was sent to pathology for frozen section, and an ovarian seromucinouscystadenoma (borderline)was confirmed. Examination of the pelvis, abdominal walls, appendices, and peritoneum was within normal limit.

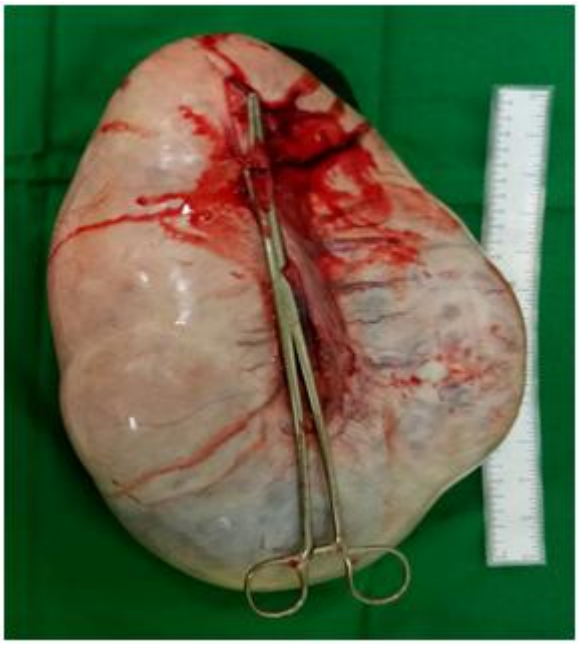

Figure 4. *A mass from left adnexa measuring 30 x 20 x 13 cm*

Specimen received in the pathology department, showedpapillary seromucinouscystadenomamultilocular with atypical proliferation (borderline). The patient was discharged on 3rdday after operation thencontinues to undergo close follow-up every three months.

3. DISCUSSION

Ovarian masses in young children are rare,they represent less than 2% of all tumors in girl less than 16 years of age.Seromucinous tumors of the ovary including borderline tumors occur in middle adult life and are extremely rare in children.[10]Although epithelial ovarian cancer is common in the adult, it identifies only 1.9% of all ovarian neoplasm in the childhood. They arise from the surface epithelium and adjacent stroma. Serous cystadenoma constitutes between 20 to 50 percent of ovarian neoplasms and mucinous cystadenoma account for 15-25%. Other epithelial tumours occur less frequently.Serous tumors were bilateralmore often (59.8%) than the rest of the tumors (mucinous tumors 13%, endometrioid 22.2% and clear cell 15.8%). Seromucinous tumorswere bilateral in four of the thirteen cases (30.8%).In 1976, Fox and Langley first introduced the word seromucinoustumour which was composed of endocervical type mucinous epithelium and serous type of cells.Later in 1988, Rutgers and Scully described similar appearing borderline tumour into two sub classes. The first was classified as “ovarian mullerian mucinous cystadenoma of borderline malignancy” which was composed of pure endocervical type of epithelium and the second one was classified as “ovarian mixed epithelial papillary cystadenoma of borderline malignancy” consisting of mixture of serous, endocervical type mucinous, endometrioid and undifferentiated cells with abundant eosinophilic cytoplasm.[5]The histologic subtypes of epithelial ovarian tumors in children are only serous and mucinous tumors, and are more commonly serous than mucinous.Histologically, seromucinous tumorswere characterized by their varietyin cell composition and by their papillary architecture characteristicoedematous papillae often filled with neutrophils.[11]In addition borderline epithelial ovarian tumors are about 70% of all epithelial neoplasm (21% of all ovarian malignancies) in women aged less than 25 years.[9]Organization (WHO) adopted the term “borderlinemalignancies” to describe these tumors. Borderlinetumors represent approximately 10–15% of all epithelialovarian malignancies, is characterized pathologically by features of malignant tumors, including cellular proliferation, stratification of the epithelial lining of the papillae, nuclear atypia, and mitotic activity, but without destructive stromal invasion.[3, 4]

Recent studies suggest the role of BRAF and KRAS mutations in the development of borderline ovarian tumors.These genes participates in mitosis pathway transduction signaling of MEK/ERK/MAPK (mitogen

extracellular signal kinase/ extracellular signal regulated kinase/ mitogen-activated protein kinase). BRAF or KRAS mutations occur in 47-60% of serous borderline tumors.[12]Seromucinous neoplasms consist of benign, borderline and malignant forms and are a new sub-category of epithelial ovarian tumours in the WHO 2014 classification. The seromucinous borderline tumour (SMBT) was previously considered as a subset of mucinous tumours (endocervical type) and accounts for 15% of mucinous borderline neoplasms; 40% of these are bilateral. Macroscopically, these tumours are unilocular with a smooth surface and friable papillary projections. Microscopically, there is similar architecture to serous borderline tumours. The larger papillae are oedematous and often contain neutrophils.The epithelium is stratified and is a mixture of endocervical-type mucinous or serous epithelium, but squamous and endometrioid epithelium can also be seen. Similarly to SBT, microinvasion, intraepithelial carcinoma and micropapillary features and peritoneal implants can be seen. The typical immunohistochemical profile is CK7+/CK20-/CDX2-. The tumours are usually ER and PR positive and negative for WT1. These tumours are associated with good outcome regardless of the presence of peritoneal implants.[13]

Seromucinous tumorsderived from the coelomic epithelium and consist of ciliated epithelialcells filled with mucin; most are benign. These cells resemblecells of the fallopian tube and endocervix or may mimic intestinal cells, whichcan pose a problem in the differential diagnosis of tumors thatappear to originate from the ovary or intestine.[14, 15]

Abdominal pain presented in cases with torsion, but many of the remaining cases only displayed abdominal enlargement, as in our case.Most of patients presented with early stage diseases. However, it is not easy to diagnose such tumors because symptoms are not typical. Preoperative diagnosis indicate suspicion of a malignancy in 80% of adolescent patients, based on imaging study and CA 125 level.CA125 has been widely used as a marker of ovarian tumors.Because CA-125 levels correlate withthe progression and regression of these tumors, it has beenuseful in tracking the effect of treatment and recurrence ofepithelial ovarian carcinoma.[2]In contrast to germ cell tumors, epithelial ovarian tumors frequently may indicate an elevation of CA 125 level. Similarly, the large mass of this case showed the possibility of malignancy with highly elevated epithelial tumor markers CA 125. Although the usual surgery for obviously benign ovarian tumors in children is performed via laparoscopy, laparoscopy is contraindicated in patients with suspicion of malignancy because of concerns regarding spillage of malignant tumor contents. The standard treatment for ovarian malignancy in them is conservative surgery followed by adjuvant chemotherapy, depending on stage and histology.According to the American College of Obstetricians and Gynecologists 2007, the recommended surgical treatment for ovarian borderline malignancy includes resection of all visible tumor tissue, an omentectomy, and an appendectomy if a mucinous tumor is present and also suggest either a unilateral salpingooophorectomy or ovarian cystectomy for fertility sparing procedures.[9, 10]In the presence of a benign or borderline unilateral ovarian mucinous tumour as defined during the operation and with normal peritoneal and appendiceal gross morphology, appendectomy is not a necessary adjunctive procedure.[16]However, fertility is an important issue for premenarchal children. The role of fertility sparing surgery has been discussed in adult cases, as the prognosis of BOT is excellent and the lesion tends to arise during the child bearing years. Some reports have compared the fertility sparing surgery with radical surgery. In those studies, the recurrence rate was somewhat higher in the fertility sparing group than in the radical surgery group. In the fertility sparing surgery group, the most common pattern of recurrence was isolated recurrence in the remaining ovaries.Cystectomy may have a greater chance of preserving fertility, but is associated with higher recurrence rates than those seen after oophorectomy. Salpingooophorectomy has thus been recommended as fertility sparing surgery. If malignancy is diagnosed, then appropriate staging biopsiesshould be performed. If the contralateral ovary appears normal, it is recommended that it not bebiopsied to avoid potential infertility caused by peritoneal adhesions or ovarian failure.[17]In our case, salpingoophorectomy was performed because intraoperative frozen section histopathological examination indicated seromucinouscystadenoma and the contralateral ovary was intact.Salpingooophorectomy or oophorectomy for premenarchal BOT appears appropriate when the operative findings reveal localized unilateral disease.[3]In our case microscopic examination of huge ovarian mass showed multilocular cyst with solid part. The cyst was coated a thorax epithelium with a

polypoid structure. In other places, it was coated cuboidal epithelium layer and several layers. The tumor was limited to the base of the epithelium and did not invade the stroma. The final diagnosis of papillary seromucinouscystadenomamultilocular with atypical proliferation (borderline) was given.

In the present case also there was admixture of serous and endocervical type of cells without any cellular atypia and stromal invasion, and hence was diagnosed as seromucinouscystadenoma. Tumors with complex papillary architecture and epithelium showing variable cellular stratification, mild to moderate cytological atypia without stromal invasion are classified as atypical proliferative or borderline tumors. Tumors with similar architecture and epithelial lining having either marked cytologicatypia or cribriform growth pattern with stromal invasion >5 mm in diameter in any focus are classified as malignant tumors.[5]Epithelial borderline tumors have an excellent prognosis and all patients with BOT or adenoma were alive without recurrence as of final follow-up.[3]However, if the tumors relapse, the five-year survival rate is approximately 81%; if the tumors become malignant, the five-year survival rate is reduced to 68%. In addition, the recurrence rate within first year after treatment in children and adolescents is about 75% and within the second year after initial treatment it is 90%. Therefore, long and careful follow-up are critical to observe for disease recurrence by surveillance pelvic imaging and tumor markers (CA 125). In the adolescent, an early diagnosis for ovarian tumors is required to determine the direction of treatment. It is important to detect the possibility of malignancy in the early due to an effect on the future fertility and ovarian function. The goals of treatment for children and adolescents are to exterminate the disease, and restore the uterus and ovarian function for conservation of reproductive potential.[9]

4. CONCLUSION

This is a rare case report of seromucinous borderline tumor in young childrenand their clinical behavior is notas aggressive as other types. On ultrasonography the origin of this mass could be delineated from ovary. Later further on CT scan it was suspected to arise from ovary, during the surgery the origin was confirmed to be from the ovary. Death related to this kind of tumor is rare. In our patient, conservative surgery was chosen because of themacroscopic appearance of a benign cyst and a girl was still 14 years old. Conservative surgery as ovarian cystectomy and salpingooophorectomy is adequate for benign lesions. Postoperatorymonitoring of patients plays a critical role in case of any possible relapses,especially consequent malignant evolutions.Prognostic factors have been studied, including morphologic cellular atypia, tumornecrosis, mitotic index, and depth of tumor invasion. On histopathological examination final diagnosis of seromucinous borderline tumor was rendered. Accurate diagnosis and clinical staginglead to better treatment results, and reduce the use ofunnecessary aggressive therapies.

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