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Case Report

Yolk sac tumour in pre-pubertal girl: a case report

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ABSTRACT

The commonest malignant ovarian tumour in the adolescent group is yolk sac tumour. It is commonly encountered in adolescents and young women. Incidence is 1% of all ovarian tumours. We reported a case of yolk sac tumour in a 9-year-old girl who presented with intermittent lower abdominal pain, not settling with medical management. Abdominal ultrasonogram showed a left adnexal echogenic mass measuring 5×6 cm with cystic spaces and internal vascularity. MRI abdomen showed T2/STIR hetero intense mass indenting the uterus and posterior bladder wall, multiple bilateral internal iliac, external iliac, left common iliac, aortic and bilateral inguinal nodes along with minimal ascites were seen. She underwent laparoscopy with trucut biopsy which showed moderate nuclear atypia with occasional Schiller-Duval body. Medical oncologist opinion was obtained and she was advised 4 cycles of chemotherapy with carboplatin, bleomycin and etoposide. Later she was planned for laparoscopic cytoreductive surgery. Laparoscopy showed rudimentary uterus, residual left ovarian mass, bilateral normal tubes and small pre-pubertal right ovary. Hence, left salpingo-oophorectomy, infra colic omentectomy and suspicious residual deposits of 1×1 cm near the right broad ligament were removed. Histopathological report of ovary showed no evidence of any residual malignancy. Peritoneum and omentum were free of tumour. Following laparoscopic cytoreductive surgery she is on follow up with AFP till date which is in declining levels and almost reached a normal value.

Keywords: Ovarian tumour, Yolk sac tumour, Germ cells tumour, Surgical management, Chemotherapy

INTRODUCTION

Yolk sac tumour (YST) is one of the ovarian germ cell tumours. It is also known as primitive endodermal tumour or endodermal sinus tumours are malignant. It has the histological similarity to the mesenchyma of primitive yolk sac.[1] The incidence is same in both boys and girls and they are very rare. They occur more commonly in pre pubertal age. YSTs predominantly arise from the gonads and rarely have extra gonadal origin.[2] 1% of all ovarian tumours are found to be YSTs. Ovarian YSTs are highly malignant, rapidly growing and have high rate of metastasis. 5 years survival rate has increased from 14% - 90% because of chemotherapy.

CASE REPORT

A 9-year-old premenarchial girl, suffered from intermittent lower abdominal pain for 1 month. There was no history of vomiting, diarrhoea, fever and burning micturition. She had consulted a paediatrician several times for similar complaints which did not settle with medical management. Ultrasound of the abdomen was suggested as pain did not subside and it showed a left

adnexal echogenic mass measuring 5×6 cm with cystic spaces and internal vascularity. Hence, the patient was referred to our hospital for further management. On examination she was conscious and oriented. There was no icterus/pallor/palpable lymph nodes/edema or cyanosis. Per abdomen examination showed a soft non tender mass palpable in the left iliac fossa. Other vital signs were normal. Magnetic resonance imaging of the abdomen and pelvis showed T2/STIR hetero intense mass indenting the uterus and posterior bladder wall, multiple bilateral internal iliac, external iliac, left common iliac, aortic and bilateral inguinal nodes along with minimal ascites were seen. There was no hydroureteronephrosis or liver nodules. Basic investigations were found to be normal and tumour markers such as CA 125, CEA, AFP, LDH and β-HCG were done. Following values were obtained: CA 125 36.0 U/ml, CEA 1.80 ng/ml, AFP >100 IU/ml, LDH-326 U/l and β-hCG <1.0.

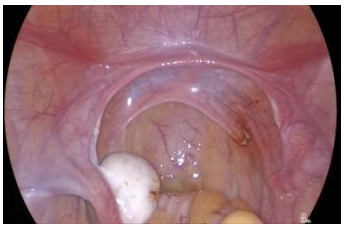

Figure 1: Pre-operative laparoscopic view.

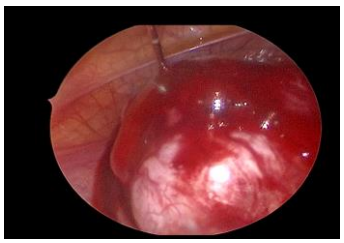

Figure 2: Trucut biopsy in laparoscopy.

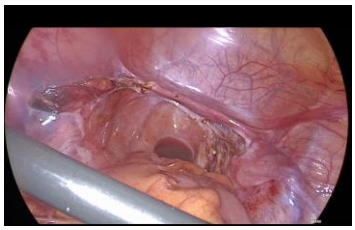

Figure 3: Final surgical view.

She was planned for diagnostic laparoscopy and biopsy. Laparoscopy showed mild ascites with a left ovarian mass. There were no peritoneal deposits. Trucut biopsy was taken from the mass. Biopsy report showed cells with moderate nuclear atypia with occasional Schiller-Duval body suggestive of YST. She was referred to a medical oncologist and was advised 4 cycles of chemotherapy with carboplatin, bleomycin and etoposide.

Later she was planned for laparoscopic cytoreductive surgery. Laparoscopy showed rudimentary uterus, residual left ovarian mass, bilateral normal tubes and small pre-pubertal right ovary. Hence, left salpingo-oophorectomy, infra colic omentectomy and suspicious residual deposits of 1×1 cm near the right broad ligament were removed. Histopathological report of ovary showed no evidence of any residual malignancy. Peritoneum and omentum showed non-specific inflammation and were free of tumour.

Post cytoreductive procedure, she underwent another 2 cycles of carboplatin, bleomycin and etoposide. She is on follow up till date.

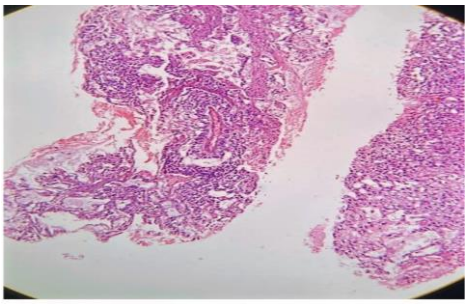

Figure 4: Histopathology.

Table 1: Summary of clinical characteristics of YST.

Summary of clinical characteristics	
Median age at presentation	18 to 25 years
Clinical presentation	Rapidly enlarging abdomino-pelvic mass
Imaging (CT scan, echography)	Large solid and cystic aspecific tumour
Tumour marker	AFP
Histology	Glomerular-like structure with a centra vessel surrounded by cuboidal cells called Schiller-Duval body. Hyaline globules, characteristic of the AFP. AFP expressed on immunochemistry
Follow up after treatment	AFP to be done every 3 months during first year and every 6 months during subsequent years

DISCUSSION

YST of the ovary, also known as endodermal sinus tumour, is the second most common malignant ovarian germ cell tumours (MOGCT), after dysgerminomas and accounts to 20% of the germ cell tumours and about 1% of all ovarian malignancies.[3,4]

They originate from the primitive germ cell and gradually differentiate to mimic tissues of either the embryonic origin like ectoderm, endoderm and mesoderm or the extraembryonic tissues like the yolk sac and trophoblast. Ovarian germ cell tumours (OGCTs) are subdivided into germinomatous and non-germinomatous tumours.[4,5] The specific type of tumour depends on the degree of differentiation. A germinoma would develop if there is no differentiation, embryonal carcinoma would develop with differentiation and YST or choriocarcinoma would develop with extra embryonic differentiation.[6] YST is usually seen in adolescents and young adults, between 18 to 30 years of age.[7]

This patient presented at the age of 9 years. The aetiology of YST of the ovary is still poorly understood. Probable risk factors are exposure to maternal exogenous hormone use or radiation exposure during pregnancies which are based on findings from studies of testicular cancer among adult populations which share similar features.[8] However, there is no confirmed risk factor for yolk sac tumours of the ovary.

Clinical symptoms include an enlarging pelvic mass which extends to the abdomen, associated with pain, and abdominal distension.[4] Fever, dyspnoea, increased body weight, and vaginal bleeding may occasionally be observed. Sometimes, patients are asymptomatic and are diagnosed incidentally. Ascites or peritonitis may be detected secondary to torsion. Duration of symptoms are usually brief with a median duration of 2 to 4 weeks. This patient presented with intermittent abdominal pain for a period of 4 weeks which did not subside with medical management. Pre-operative clinical or radiological diagnosis is difficult to make. Imaging studies include abdominal or transvaginal ultrasound, CT scan, or MRI. Large solid tumours that can be cystic, with signs of hyper vascularization and areas of haemorrhage are described.[7] However, no specific imaging has been described to distinguish YST from other ovarian masses preoperatively.[10] MRI showed T2/STIR hetero intense mass indenting in the uterus and posterior bladder wall (likely to be malignant ovarian mass lesion). There were multiple bilateral internal iliac, external iliac, left common iliac, aortocaval and bilateral inguinal nodes along with minimal ascites without hydroureteronephrosis or liver nodules.

Tumour markers showed the following values. CA 125 36.0 U/ml, CEA 1.80 ng/ml, AFP >100 IU/ml, LDH-326 U/l and β-hCG <1.0. Out of these tumour markers, serum alpha-feto-protein (AFP) level is the hallmark of this tumour. It is also a useful marker for the diagnosis and follows up of YST for complete remission or recurrence. Serum AFP levels are elevated in all patients with tumours containing YST components at diagnosis.[11] Prognostic value of high level of AFP at diagnosis remains controversial. In two studies, AFP >1000 kU/l was associated with a higher risk of relapse.11 Two other authors found that pre-operative serum AFP levels before initial surgery had no significant correlation with prognosis.[12] Decreasing levels of post-operative serum AFP is an effective indicator to determine whether residual disease remains or not after surgery or after chemotherapy.[13] In order to detect relapse, AFP is more sensitive than computed tomography scan (CT scan).[14]

Histopathology confirms the diagnosis. On gross examination, YSTs are soft, solid masses, tan to yellow or grey in colour with a mucoid appearance, necrotic, cystic changes, and hemorrhagic. Though they are encapsulated occasional herniation or rupture can be observed. On cut section, they are rarely unicystic or uniformly multicystic but they also contain solid areas composed of soft white-grey and yellow-brown heterogeneous tissue with foci of haemorrhage and necrosis. Microscopically, various histological patterns may be present. The most typical histological feature is a glomerular-like structure with a central vessel surrounded by prominent large cuboidal cells called the Schiller-Duval body.[15] They are cellular structures that resemble fetal glomerulus, pathognomonic of endodermal tissue. Nevertheless, this pattern was present in only 20% of cases. Hyaline globules, characteristic of the AFP synthesizing cells found in YST are described inside the cells with periodic-acid-Schiff (PAS) stain. Their presence can be regarded, therefore, as a diagnostic clue to YST in an appropriate clinical setting and in the presence of AFP production.[16] Nowadays, immunohistochemical markers are of high value in the accurate diagnosis of these tumours. On immunohistochemistry YST typically express AFP and are consistently positive for cytokeratines.[17] They lack oestrogen and progesterone receptors. Placental-like alkaline phosphatases are found in 50% of cases. Histological examination of ovary showed no evidence of any residual malignancy which proved that the tumour is chemo responsive. Peritoneum and omentum showed non-specific inflammation, free of tumour.

Chemotherapy has dramatically changed the prognosis of these malignancies; Five-year survival rate has increased from 14% to nearly 90%.[12] Bleomycin, etoposide, cisplatin (BEP) chemotherapeutic regimen has proved to be efficacious in treating MOGCTs. After surgical resection, the national comprehensive cancer network recommends, 3 to 4 BEP cycles depending upon the residue, metastatic stage, and high post-operative AFP level. This patient received 4 cycles of chemotherapy with carboplatin, bleomycin and etoposide before surgery and 2 courses after surgery.

Toxicities such as hair loss, fatigue, nausea, and myelo suppression have been reported with BEP regimen.[18] Cisplatin is known to be associated with nerve damage manifesting as peripheral neuropathy or hearing loss. A potentially fatal side effect of this regimen is bleomycin induced pulmonary fibrosis, making it mandatory for patients to have pulmonary function testing before treatment to document baseline function and allow for surveillance of function during therapy. In addition to that,

we have to pay attention for secondary malignancy related to etoposide like acute myelogenous leukaemia, related to cumulative dose effect.[18] Though there is concern of risk of infertility following chemotherapy, the majority of these patients will maintain their ovarian function and fertility, as reported in various studies.[5] This particular patient though she had the other ovary, her uteruswa pre-pubertal in size and hence we had to wait and watch for menarche to occur.

The stage distribution at diagnosis was particularly different from that of epithelial tumours. Approximately 60% to 70% of tumours are International Federation of Gynaecology and Obstetrics (FIGO) stage I or II, 20% to 30% are stage III, stage IV is relatively uncommon (Table 1).[19] Bilateral ovarian involvement is rare. For this patient staging was probably stage 1.

The standard management of malignant ovarian germ cell tumours was complete surgical excision followed by adjuvant chemotherapy.[3,5] Fertility-sparing surgery is often possible, as the tumours are unilateral.[5] Recently, minimally invasive surgery has been recommended for better prognosis. Nishio et al had reported prognostic factor for patients with MOGCTs was based on surgery either conservative and fertility sparing, followed by needed adjuvant chemotherapy.[18,20] Even in patients with bulky metastasis, normal appearing uterus and contralateral ovary can be safely preserved for future fertility.[18] However, it is recommended that patients with bulky disease in the abdomen, pelvis, and retroperitoneum should be surgically cytoreduced to optimize the residual disease if possible.

The principles of cytoreductive surgery had to be followed which includes hysterectomy, bilateral salpingo-oophorectomy (BSO), peritoneal cytologic studies, omentectomy and multiple biopsies of the pelvic and abdominal peritoneum and the retroperitoneal lymph nodes. In patients needing fertility preservation, unilateral salpingo-oophorectomy can be done with multiple peritoneal biopsies. Prognosis is based on tumour stage and the residual volume of disease.[12] With the advent of chemotherapy, the extent of the surgical procedure required has progressively been reduced and becomes more restrictive, thereby allowing, whenever possible, preservation of fertility. Gershenson et al in a review concluded that for most patients with OGCT, unilateral salpingo-oophorectomy with preservation of the contralateral ovary and the uterus was appropriate.[21] Nawa et al demonstrated no significant difference in 5 year-survival rate between patients who underwent fertility sparing surgery and patients who underwent more radical surgery.[12] The difference in 5-year survival rate with and without node dissection was not significant either. In the study of Fujita et al (41 YST), Mitchell et al (45 YST over 69 OGCT) and Mayordomo et al (11 YST over 33 OGCT), the outcome of patients treated by unilateral salpingo-oophorectomy was the same as that for patients treated by more aggressive surgery.[11] Components of standard surgical staging include peritoneal washing and multiple biopsies of the pelvic and abdominal peritoneum and the omentum. Debulking surgery remains important, the prognosis being affected by the residual tumour.[12] A second look laparotomy (SLL) as demonstrated by Mitchell et al the routine use of second-look surgery after chemotherapy was unnecessary.[11] None of the 24 patients who underwent second-look surgery had evidence of active tumour. In the US, the Gynaecologic Oncology Group (GOG) reviewed their experience for patients treated with platinum-based regimens, and they concluded that a post chemotherapy surgical reassessment was of negligible benefit

There is no discussion regarding the role of laparoscopy in all these studies. More over YST usually present as solid large tumours (median tumour diameter of 20 cm) and resection by laparoscopy may not be feasible. If resection is feasible, usual precautions as the use of endo bags should be applied to prevent port site metastases.

This patient was planned for laparoscopic cyto-reduction. Laparoscopy showed rudimentary uterus, residual left ovarian mass, bilateral normal tubes and normal right ovary. Hence, left salpingo-oophorectomy done along with the mass, infra colic omentectomy and residual deposits of 1×1 cm near the right broad ligament were also removed using endo bags.

Stage I disease, less than 42 days to AFP normalization has good prognosis.[5] Progressive or recurrent ovarian tumour after treatment with BEP chemotherapy has been reported to be associated with a poor prognosis.[5] As there are no approved chemotherapy schemes in such cases, the possible options include combination of vinblastine, ifosfamide, cisplatin, or paclitaxel and ifosfamide, cisplatin, as adapted from the regime for testicular cancer.[5] Second look cytoreductive surgery may be of use in chemo resistant tumours.

As a follow-up of chemotherapy, AFP should be repeated before each cycle of therapy, soon after the end of the treatment, every three months the first two years, then every six months from the third to the fifth year, and once a year after the end of chemotherapy.[4,22] An annual clinical examination and a pelvic ultrasound is necessary in the case of conservative treatment, to screen for a contralateral recurrence.

CONCLUSION

Yolk sac tumour occur in <1% of ovarian tumours mostly in adolescent and young women. Lower abdominal pain in adolescent girls not responding to medical management with adnexal masses, we have to think about germ cell tumour. Management is usually removal of the ovary followed by chemotherapy. In this patient since there was evidence of nodal involvement and minimal ascites, laparoscopic biopsy of the mass was done to get histopathological confirmation which showed yolk sac

tumour. Schiller-Duval bodies are the typical histopathological feature. 4 cycles of chemotherapy was given with carboplatin, bleomycin and etoposide. Following chemotherapy, conservative cytoreductive surgery along with infra-colic omentectomy was done. There was no residual malignancy in the surgical specimen. AFP is the main tumour marker which has to be followed up in post-operative period. Patient received two more cycles of chemotherapy and tumour markers becomes negative. Patient has to be followed up every 3 months for 1st 2 years and there after every 6 months. Annual examination and pelvic USG should be done whenever conservative surgery was done.

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