VOLUME - 12, ISSUE - 04, APRIL - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Obstetrics & Gynaecology

# METASTATIC YOLK SAC TUMOUR: A DIAGNOSTIC DILEMMA CASE REPORT AND LITERATURE REVIEW


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**KEYWORDS :**

## INTRODUCTION:

Ovarian germ cell tumors (OGCTs) account for about 15–20% of all ovarian neoplasms[1]. Malignant ovarian germ cell tumors (MOGCTs) are rare, accounting for 3–5% of all malignant ovarian neoplasms[2]. Yolk sac tumor (YST) also referred to as endodermal primitive tumor is the second most common tumor in MOGCTs.[3] YST accounts for 20% of MOGCTs and commonly affects young women and adolescent girls between 18-30 years of age. Around one third of YSTs affect premenarchal girls.[1] When compared with epithelial ovarian tumors, YST is highly malignant with a propensity for rapid growth and acute development of symptoms. YSTs rapidly metastasize, intruding all intra-abdominal structures as well as retroperitoneal lymph nodes.[4] Before the advent of combination chemotherapy, YSTs were associated with poor prognosis. The introduction of novel chemotherapeutic regimens has been associated with significantly improved 5-year survival rates of YST from 14% to nearly 90%.[5] The prognosis even for the advanced stages has remarkably improved with the addition of cisplatin to the chemotherapy regimens.[6]

## Case Report:

We report the case of a 30-year-old woman, P1L1 presenting to our Gynecological OPD with complaints of progressive pain abdomen, nausea, vomiting, loss of appetite and weight loss for past two months. She also complained of on and off episodes of high-grade fever, which was associated with chills. General examination revealed mild pallor. On abdominal examination, hepatomegaly and lower abdominal fullness were noted. On per vaginal examination uterus was anteverted and normal sized, left fornix was free and a cystic mass of ~8x8 cm was felt in the right adnexa, which had regular surface and restricted mobility.

During hospital stay, the patient had multiple episodes of high-grade fever, which was not responding to paracetamol. All the blood work and cultures came negative and the fever responded to naproxen.

The clinical examination was supplemented by ultrasound of the abdomen and pelvis, which showed hepatomegaly (16.9 cm) along with multiple ill-defined lesions predominantly in the left lobe and a 10.4x6.7 soft tissue density lesion in the left adnexa with cystic areas within and internal vascularity. CECT whole abdomen reported a 10.2x11.9 cm mass in the right adnexa, likely arising from ovary along with multiple heterogeneously enhancing mass lesions in both lobes of liver, largest 4x3cm. Tumour marker panel depicted elevated AFP (>1210ng/mL). FNAC liver suggested hepatocellular carcinoma. Trucut biopsy from ovarian mass was inconclusive. Initial diagnosis of hepatocellular carcinoma was considered after consultation with the Gastrosurgery Department. The patient was started on Sorafenib, which was given for 3 cycles but the tumour failed to respond to the regimen. A repeat trucut biopsy from the ovarian mass was taken which came positive for AFP and Glypican 3 on IHC, suggesting yolk sac tumor. The diagnosis was revised to Stage 4B ovarian YST. Due to extensive spread of the tumour an initial combination chemotherapy of 4 cycles of Bleomycin-Etoposide-Cisplatin followed by 2 cycles of Etoposide-Cisplatin was given. Repeat imaging showed decrease in size of lesions and a falling AFP trend observed, with a value of 7.5ng/mL after 4 cycles of BEP. The patient then underwent staging laparotomy with total abdominal hysterectomy with bilateral salpingo-oophorectomy, left lateral sectionectomy of liver alongwith bilateral pelivic and paraaortic lympha denectomy. HPE confirmed metastatic yolk sac tumor. Post operatively 4 cycles of Etoposide-Cisplatin and 7 cycles of Etoposide given. 6 months post the last cycle of chemotherapy PETCT showed no evidence of tumor and AFP level was 1.4 ng/mL. The patient is on regular follow up and doing well.

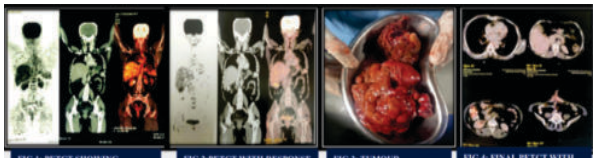

FIG 1: PETCT SHOWING UPTAKE IN LIVER & PELVIS | FIG 2:PETCT WITH RESPONSE POST BEP+EP REGIMEN | FIG 3: TUMOUR REMOVED AT SURGERY | FIG 4: FINAL PETCT WITH NO EVIDENCE OF TUMOUR

## DISCUSSION:

The yolk sac tumor is a malignant tumor resembling the yolk sac, allantois and extraembryonic mesenchyme. YSTs are mostly unilateral having a diameter of 5 cm to 50 cm. As it is a rapidly growing tumour, it commonly presents as acute abdomen due to torsion or rupture, often necessitating emergency surgery.[7] Other associated symptoms include abdominopelvic distension, ascites and fever.

Liver metastasis is a common phenomenon, especially in advanced stages (48-73%). Lymph node and lung metastases are also frequently seen in the later stages, with rates of 62% and 41% respectively.[8]

Various imaging modalities help in diagnosing YST. Ultrasound is the first line modality as it helps in characterization of an adnexal mass and can even detect ascites and hepatic metastasis. CT scan helps in evaluating spread of the tumour and involvement of the retroperitoneal lymph nodes. MRI can provide better information regarding

the characteristics of the mass, showing the hypervascularized and haemorrhagic areas.[9]

YSTs grows in a confusing variety of histologic patterns which can lead to dilemma in diagnosis and delay in treatment. Immunohistochemical staining has an important role in establishing timely diagnosis. The most useful stain is for α-fetoprotein, a specific tumour marker for YST with more than 75% positivity rate. AFP is also a very useful tool in the follow up of these patients, especially to detect existence of residual neoplastic cells post-surgery. Glypican-3 has recently emerged as an additional tool for diagnosis, as more than 95% of YSTs demonstrate strong positive cytoplasmic staining.[10]

The surgical procedure previously used to be extensive involving hysterectomy, adnexectomy, omentectomy and lymphadenectomy for all patients, irrespective of the stage of the disease. However, in 1976 in a series of studies involving ovarian endodermal tumours, it was proven that adnexectomy had equivalent results when compared to extensive surgery in patients with stage I of yolk sac tumor.[5,11] It has also now been proven that systemic lymphadenectomy does not affect the five-year survival rate.[11,12]

Chemotherapy has significantly improved the prognosis of these malignant tumors; the five-year survival rate increasing from a mere 14% to as high as 90%.[5] The BEP protocol (Cisplatin, Etoposide, Bleomycin) which has been the standard treatment of testicular germinal tumors showed an efficacy equivalent to the PVB protocol (Cisplatin, Vinblastine, Bleomycin) in treating YSTs and has been associated with less toxicity.[13] Since its implementation, several studies have demonstrated the effectiveness of the BEP protocol in ovarian germ cell tumors, having a five-year survival rate nearing 94% for all stages.[11,12] Recent NCCN guidelines recommend 3 to 4 cycles of the BEP regimen (4 cycles minimum in the presence of poor prognostic factors).

The overall survival in various studies has been shown to be influenced by various factors like the presence ascites at the time of diagnosis, stage at presentation, type of surgery and initial level of AFP. In the study of Nawa et al., the 5-year survival rate was 95.2, 75, 30, and 25% for patients with stage I, II, III, and IV, respectively.[5] The respective numbers in the study by Kawai et al. were 92, 44, and 29% for stage I, II, and III.[14] According to these two studies, other than the stage of ovarian YST, significant prognostic factors were the presence and quantity of ascites before initial surgery and the amount of residual disease after surgery.

The standard of care in MOGCTs remains fertility sparing cytoreductive surgery (FSCS) followed by adjuvant chemotherapy if required. NACT followed by interval FSCS can be a considered a reasonable option in patients with extensive disease when optimal cytoreduction or fertility sparing may not be possible.[15] The same can be considered in patients with poor general condition or clinical findings which will result in an increased risk of surgical morbidity.

In a series of 33 patients with advanced MOGCT Bafna et al. treated 3 cases with NACT followed by interval debulking with all having sustained complete response.[16] Raveendran et al. used NACT to treat 2 cases of advanced MOGCT. No residual tumor was identified during interval debulking.[17] Gueye et al. in their study treated 3 patients with NACT reported that prolonged complete response was attained following NACT and conservative surgery.[18]

In a Children's Oncology Group (COG) study for patients with advanced MOGCT rendered unsuitable for fertility sparing surgery — four cycles of chemotherapy followed by surgery demonstrated good outcome.[19] In the study by Talukdar et al , achievement of complete response in 16 of 21 patients with MOGCTs post NACT and interval debulking was observed.[20]

As evidenced by these studies, NACT followed by interval debulking in MOGCTs though not the standard of care, offers several advantages and deserves further study.

Our case reflects that even in advanced stages of presentation like stage 4 of YST, positive treatment outcomes can be successfully achieved through neoadjuvant chemotherapy and surgery. Early preoperative verification of the histology of the tumour is also a major aspect for successful treatment.

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