International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622
© Gynaecology Journal
www.gynaecologyjournal.com
2020; 4(6): 279-281
Received: 12-08-2020
Accepted: 19-09-2020

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Case Report: A case of mixed malignant ovarian germ cell tumour

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DOI: https://doi.org/10.33545/gynae.2020.v4.i6e.765

Abstract
Background: Malignant mixed ovarian germ cell tumour is a relatively rare tumour affecting young girl. It may be a threat to her future scope of fertility.
Case: A 13 years old girl reported with a large abdomino-pelvic mass along with enlarged para-aortic lymph nodes and raised beta-hCG, alfa-feto protein and lactate dehydrogenase levels. Fertility sparing surgery followed by four cycles of adjuvant chemotherapy was given to her. Her one year follow-up has been recurrence free.
Conclusion: Advanced malignant mixed ovarian germ cell tumour can be treated by fertility preserving cytoreductive surgery and adjuvant chemotherapy with good outcome.

Keywords: mixed malignant ovarian, germ cell tumour, adjuvant chemotherapy

Introduction
Malignant ovarian germ cell tumours account for approximately 2% -3% of all ovarian tumours with an estimated incidence of 0.5 per 100,000 women [1]. They arise from primordial germ cells derived from the embryonal gonad. Mixed malignant germ cell tumours of the ovary is a distinct entity amongst the malignant ovarian germ cell tumours. They contain two or more different types of germ cell neoplasm which is either intimately mixed together or existing as separate foci. They accounted for only 8% of malignant ovarian germ cell tumours [2].

Case Report
A 13 years old average built girl reported with dull aching pain in her lower abdomen along with a gradually increasing abdomino-pelvic mass for the last one month. There was no associated history of any vomiting, fever, menstrual, bowel or micturation problem. She attained her menarche at 12 years of age and there was no feature of any sexual precocity. There was no co-morbid factor or history of any previous surgery. On examination, there was a non-tender, mobile abdomino-pelvic mass corresponding to approximately 28 weeks gestational size. Her CECT scan revealed 18 x 20 cm sized ovarian mass with solid and cystic components along with multiple enlarged para-aortic lymph nodes. Her tumour markers showed beta-hCG (beta human choriongonadotropin) of 1457 IU/mL, AFP (alpha fetoprotein) of 41,000 IU/mL and LDH (lactate dehydrogenase) of 4415 IU/mL**.** We did a fertility preserving cytoreductive surgery which included peritoneal wash cytology, right salpingo-ophoorectomy, right pelvic lymphadenectomy, para-aortic lymph node sampling of the enlarged lymph nodes, multiple peritoneal biopsies of the para-colic gutters, pouch of douglas, vesico-uterine peritoneal surface and omental biopsy of the portion of the omentum which was found attached to the tumour mass. Intra-operative findings showed a normal left tubo-ovarian complex and there were no other metastatic deposits in the abdomen. Her histopathological report showed malignant mixed ovarian germ cell tumour with yolk sac component of 40 %, dysgerminoma component of 40% and choriocarcinoma component of 10%. There was no immature teratomatous component. Although there was no positive pelvic lymph node but with three positive para-aortic lymph nodes; she had been assigned as a patient of Stage III C malignant mixed ovarian germ cell tumour. Post-operatively, she received four cycles of BEP (Bleomycin, Etoposide and Cisplatin) chemotherapy. Three monthly reviews for the last one year showed good outcome with no signs or symptoms of recurrence.

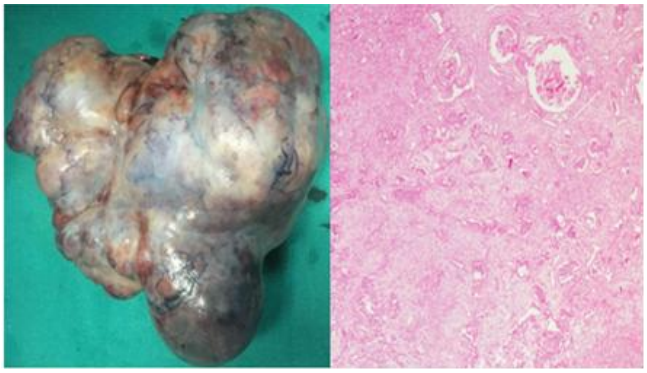

Fig 1: Gross & Microscopic view of the mixed malignant ovarian germ cell tumour

Discussion

Malignant mixed ovarian germ cell tumours are large, unilateral neoplasms. In one series of report, the component in malignant mixed germ cell tumour was dysgerminoma (80%), endodermal sinus tumour (70%), immature teratoma (53%), choriocarcinoma (20%) and embryonal carcinoma (16%) [2, 3]. The most frequent combination has been dysgerminoma and endodermal sinus tumour. Thus, these tumours secrete different tumour markers like AFP, beta-hCG, LDH in varying proportions [4]. In contrast to a malignant mixed ovarian germ cell tumour; an immature teratoma is associated with normal tumour markers unless it is associated with mixed ovarian germ cell tumour. Embryonal carcinoma can secrete both beta-hCG and AFP, but most commonly produce beta-hCG [4]. Ca -125 can also be nonspecifically elevated in patients with malignant mixed ovarian germ cell tumours. It is generally unilateral unless the dysgerminoma component is present in a very large proportion. It is to be noted that in 10% cases; benign cystic teratoma may be found co-existing in the affected ovary or in the normal ovary [5].

Dull aching abdominal pain associated with a palpable abdomino-pelvic mass is the usual presentation. But it may present with acute abdominal pain due to torsion, haemorrhage or rupture of the tumour. Fever, vaginal bleeding and abdominal distension may also be present at times. Isosexual precocity may be evident in malignant mixed ovarian germ cell tumour due to the beta-hCG component. Stage I is the most common presentation (60%-70%) and is followed by stage III in 25%-30% cases [6]. According to a population based study almost 40% of patients with malignant ovarian germ cell tumours have advanced stage disease on presentation [7].

As this tumour mainly affects the young girl; feasibility of fertility preserving surgery is the essential exponent in its management. Unilateral salpingo-oophorectomy with conservation of the other ovary and uterus should be exercised. It is to be noted that there is no evidence that a complete para-aortic and/or pelvic lymphadenectomy is advantageous. However, in case of dysgenetic gonads or clinically hermaphrodite; one should do a bilateral salpino-oophorectomy. Pre-operatively, a karyotypic examination is essential in such cases [8].

It is presumed that the ovarian germ cell tumours have a greater propensity to spread to the lymph nodes and also hematogenously to liver or lung more than that of epithelial ovarian tumours. The extent of primary cytoreductive surgery is debatable but it should be kept in mind that there is a scope of fertility sparing surgery even in advanced cases as these tumours are highly chemo sensitive [8, 9]. Achieving an optimal cytoreduction followed by adjuvant chemotherapy leads to better progression free survival and may even lead to curative outcome [10]. It is also to be noted that macroscopic residual disease following primary cytoreductive surgery is not associated with worse prognosis even in patients with advanced stage malignant ovarian germ cell tumours [11]. In the MITO (Multi-center Italian Trials in Ovarian Cancer) trial, there has been no association between residual disease and recurrence risk [12]. Prognosis depends on identifying different components and hence a thorough tissue sampling is essential. But the anticipated risk of relapse after surgery alone (without adjuvant chemotherapy) in patients with advanced disease is as high as 75% to 80%. The most important prognostic features are the size of the primary tumour and the relative amount of its most malignant component [3]. Currently, the most common and successful adjuvant chemotherapy used in malignant germ cell tumour is four cycles of BEP regime (Bleomycin, Etoposide and Cisplatin) regardless of the tumour volume [10]. Even in advanced disease, high dose chemotherapy and stem cell rescue has shown no benefit over the usual BEP regime [13]. Presently, therapy longer than four cycles of BEP chemotherapy after cytoreductive surgery is no longer supported by various trials. Follow-up is done by assessment of tumour markers and monitoring the toxicities of chemotherapy. Febrile neutropenia is a frequent complication during chemotherapy and requires hospitalization, administration of granulocyte-colony stimulating factor (G-CSF) and broad spectrum antibiotics. After completion of adjuvant chemotherapy, there may be a small percentage of patients with residual mass. In most of the cases, such residual masses represent desmoplastic fibrosis but can be differentiated from an active residual malignant disease by tumour markers and a PET-CT scan. A localized active residual mass can be resected out surgically after due scrutiny. If there has been an immature teratomatous component in the original tumour; then there is possibility of residual malignant lesions and in such cases there is a role of second-look laparotomy. A small percentage of patients may present with active residual or recurrent disease and which can be either platinum sensitive or platinum refractive. They should be treated in specialized oncology centers and trials with high dose carboplatin, etoposide and with or without cyclophosphamide or ifosfamide and stem cell rescue if required. Also gemcitabine and oxaliplatin has shown good response in such recurrent events [13]. Overall, the prognosis of malignant mixed ovarian germ cell tumour is good after fertility preserving cytoreductive surgery and four cycles of BEP adjuvant chemotherapy.

Conflict of Interest

No sponsor or financial support has been taken from any source. There is no conflict of interest.

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