Medical Science

pISSN 2321–7359; eISSN 2321–7367

A lethal encounter with malignant mixed germ cell tumour in an adolescent girl: A double trouble

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To Cite:
Andela M, Dewani D, Mahajan K, Jajoo S, Cherukuri S. A lethal encounter with malignant mixed germ cell tumour in an adolescent girl: A double trouble. Medical Science 2022; 26:ms313e2320.
doi: https://doi.org/10.54905/disssi/v26i125/ms313e2320

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Peer-Review History
Received: 27 May 2022
Reviewed & Revised: 02/June/2022 to 23/July/2022
Accepted: 26 July 2022
Published: 27 July 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

Ovarian carcinomas are rarely encountered among paediatric population. Malignant germ cell tumours are comparatively uncommon ovarian neoplasms constituting less than 5%. Germ cell tumours consisting of numerous types, mainly including teratomas and dysgerminomas, accounts for around 10-15 % of ovarian tumours. Germ cell tumours are found to represent the malignant transformation of primordial germ cells. We discuss a case of 11 year-old girl who was been referred to our rural tertiary care centre with complaints of excruciating abdominal pain associated with abdominal distension. Patient was investigated elaborately and was found to have abnormally elevated tumour markers. Her CECT revealed an enormous tumour mass covering the entire pelvic region. Timely intervention was carried out by performing a cytoreductive surgery followed by frozen section evaluation which confirmed mixed germ cell tumour. Histopathological examination which was carried out elaborately has revealed the tumour was in advanced stage. Then the patient was started on chemotherapy. This case emphasizes that though mixed germ cell tumour among adolescents is rare condition, it is extremely important for the clinicians to be vigilant as it is often mismanaged especially in the rural centres where there is to dearth of resources and investigations.

Keywords: ovarian neoplasms, mixed germ cell tumour, adolescents, yolk sac tumour, dysgerminoma

1. INTRODUCTION

Ovarian neoplasms are comparatively rare among paediatric population. The annual incidence estimated to be around 2.2 cases per 100,000 girls. Among them, in females younger than 15 years about one quarter (27%) of all ovarian tumours is described to be malignant (Taskinen et al., 2015). However, ovarian carcinomas represent about 1.1% of all childhood malignant tumours (Young and Miller, 1975). Germ cell tumours of ovary constitute around 16-21% of ovarian neoplasms. Malignant germ cell tumours comprise of less than 5% of

all ovarian neoplasms (Koshy et al., 2015). Germ cell tumours often occur prior to puberty or in early adulthood. At all ages, the germ cell tumours comprise of various types, including dysgerminomas and teratomas, accounting for about 15 % of all ovarian tumours. They represent the malignant transformation of primordial germ cells at various stages of differentiation. The exception to this is mature benign teratoma. The diagnosis is generally starts as a suspicion on physical examination, which mainly depends on transvaginal or pelvic USG.

The detection of a large voluminous ovarian mass is found to be responsible for abdominal swelling and discomfort. However, the diagnosis is re-confirmed following the initial surgical intervention. Several tumour markers such as alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) contribute not only to the diagnosis but also for further prognosis and follow-up of the condition (Koshy et al., 2015).

Malignant germ cell tumours (GCTs) are found to be more common than sex cord stromal and epithelial neoplasms among adolescent age group which is in contrast with adult ovarian neoplasm distribution (Baert et al., 2016). Despite of the advancement in understanding the etiopathogenesis of malignant ovarian germ cell tumours, its aetiology still remains not well understood (Chen et al., 2005).

2. CASE DESCRIPTION

A 11 year-old girl presented to the Department of Emergency Medicine with history of weight loss since 6 months along with chief complaints of abdominal distension since 4-5 days and pain in lower abdomen since 3-4 days which was radiating to the back. Patient also had complaints of nausea, fever and loss of appetite. Patient was yet to attain menarche. There was no tuberculosis, breast, ovarian or colon carcinoma history in the family. Her examination findings were as follows: on general examination, pulse - 126 beats per minute, blood pressure- 100/70mmHg, weight – 29 kgs, height 135 cms, pallor present, no oedema, no lymphadenopathy. Breath sounds appeared normal and also other systemic examination was found to be within the normal limit. Tanner staging of pubic hair and breast were that of stage 2 each.

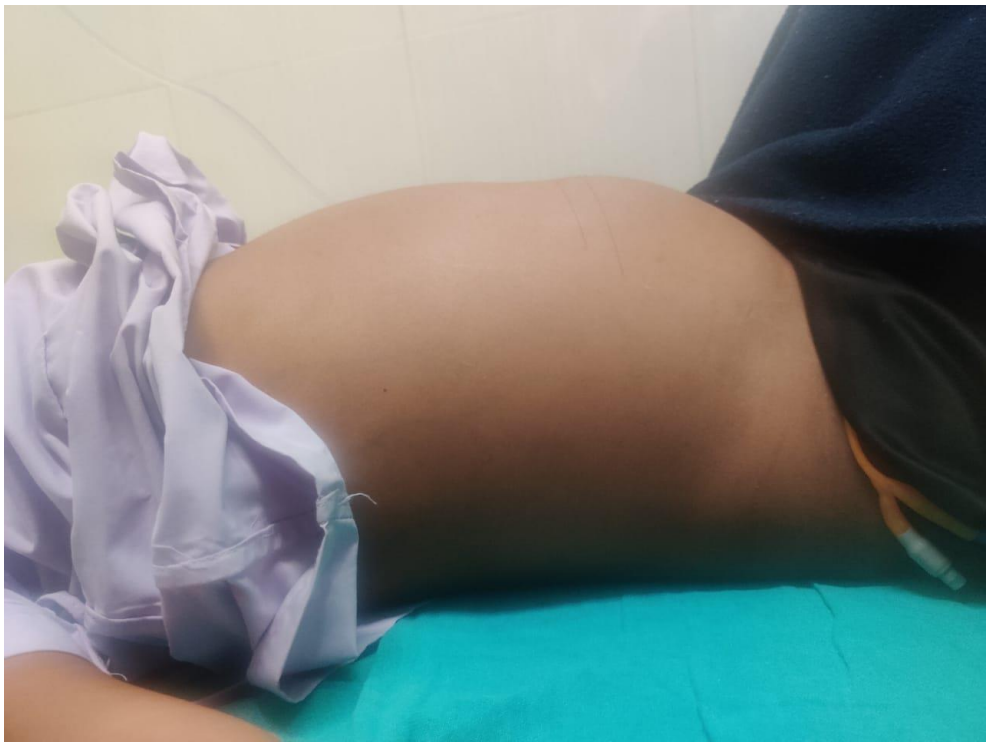

Figure 1 Irregular enlargement of abdomen with eversion of umbilicus

On abdominal examination

There was an irregular enlargement of abdomen with swelling being well appreciated more towards the right side. Figure 1 demonstrates irregular enlargement of abdomen with eversion of umbilicus.Umbilicus appeared everted with no visible engorged vessels. On palpation, mass is felt measuring about (20x15x10 cms) in size, reaching 3 cms beyond the umbilicus, firm in

consistency, having an irregular surface, ill-defined margins with restricted mobility and tenderness all over it. No organomegaly felt. On percussion dull note was heard over the mass. No bruit was appreciated over the mass.

Her tumour markers were as follows: AFP (ALPHA FETOPROTEIN) 520 mIU/ml; LDH 911 U/L; CA 125 909 U/ml; BHCG (beta human chorionic gonadotropin) 3.32 mIU/ml

Ultrasonography showed large multi lobulated predominantly solid lesion (15x12.5x8.5 cm) in pelvis with anechoic cystic areas within. Lesion showed minimal peripheral and central vascularity on Doppler. There was no evidence of any calcification. Moderate ascites was noted. CT-scan revealed large multi lobulated heterogenous solid cystic lesion (15x12x8cm) with poorly defined margins and thin enhancing septae and solid component in the pelvis extending into the abdomen mostly likely of ovarian origin? Germ cell tumour gross ascites and minimal right sided pleural effusion noted. Subcentimetric to centimetric lymph nodes noted in the mesenteric region. Figure 2 shows CECT pelvis showing huge mass in pelvis and Figure 3 demonstrates CECT abdomen showing fluid in peritoneal cavity.

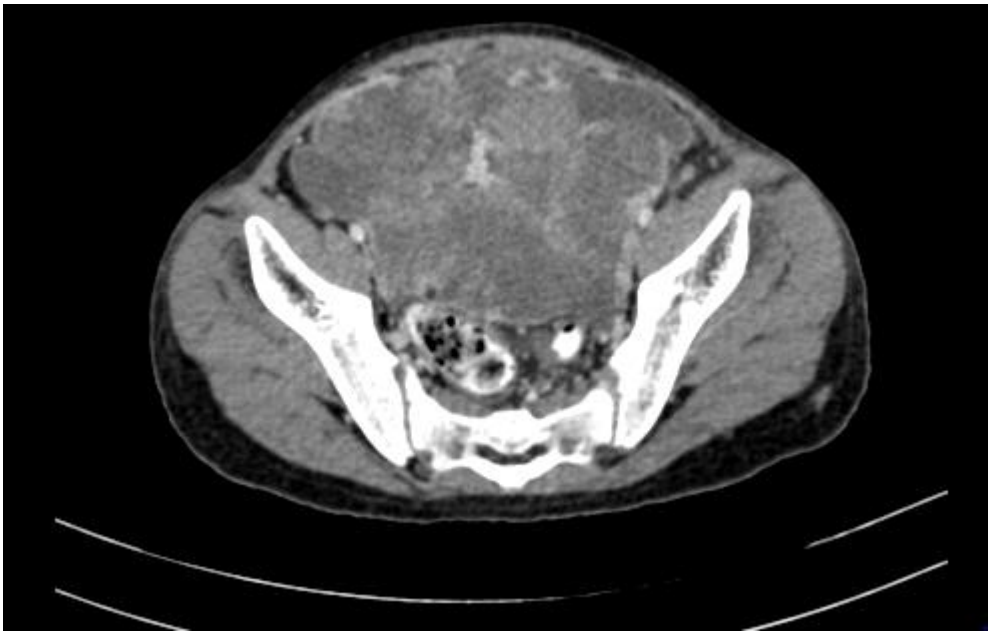

Figure 2 CECT pelvis showing huge mass in pelvis

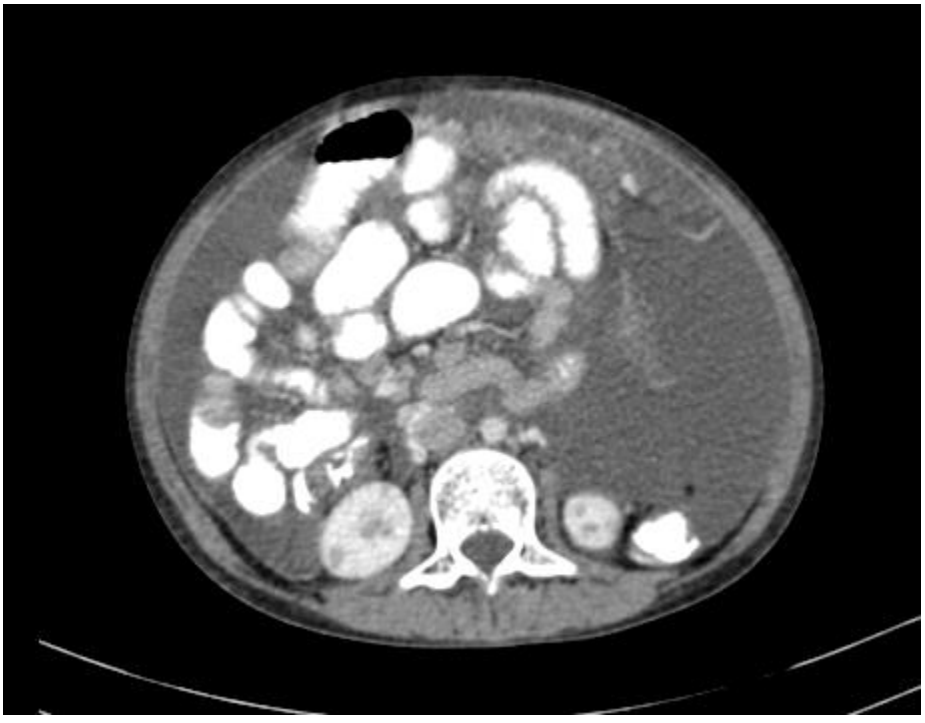

Figure 3 CECT abdomen showing fluid in peritoneal cavity

Patient was then advised pig tail catheter insertion for drainage of ascitic fluid, which was straw coloured and around 2000 ml over a time period of 72 hours with strict monitoring of her vitals and adequate hydration. Figure 4 shows pig tail catheter assisted drainage of ascitic fluid. It was done by Interventional radiologist under aseptic precautions and the procedure went uneventful. Ascitic fluid was sent for cytological examination and cell block analysis. The cell block study showed material from mixed germ cell tumour (dysgerminoma and yolk sac). Pre-operatively, the patient underwent HRCT thorax to rule out lung metastasis.

Figure 4 Pig tail catheter assisted drainage of ascitic fluid

Management

Patient's profile was discussed in the Institutional tumour board and decision of Exploratory Laparotomy (primary cytoreductive surgery) with intra-op frozen section

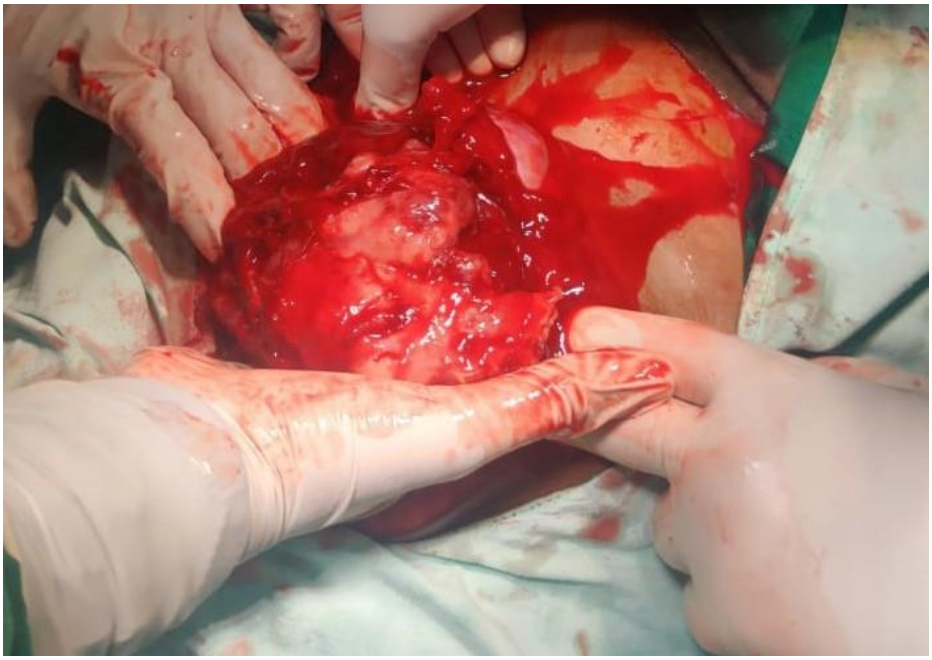

Figure 5 Solid irregular friable mass with haemorrhagic areas

Intra-op findings: On laparotomy, a yellowish white lump measuring about 23x15x12 cms friable with solid consistency with haemorrhagic areas was seen on right side. Figure 5 shows Solid irregular friable mass with haemorrhagic areas and Figure 6 showing mass with variegated areas of haemorrhage and necrosis. The lump was reaching above the umbilicus and was found to be adherent at multiple places; on its right border, near the sigmoid colon and partly at the transverse colon.

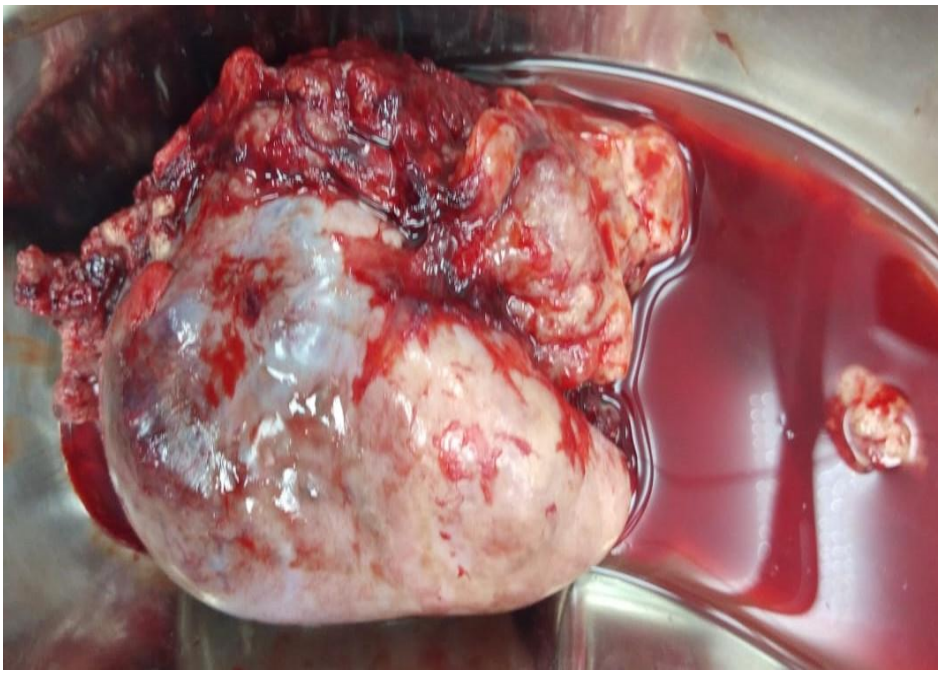

Figure 6 Mass showing variegated areas of haemorrhage and necrosis

The omentum was found to be adherent to the mass. Adhesiolysis done and the mass was then excised and delivered out and sent for further examination by frozen section. On frozen section it revealed features suggestive of Dysgerminoma. Total omentectomy was performed. Multiple Deposits were seen on the left pelvic peritoneum, on mesentery. Peritonectomy were done. Right sided salpingectomy was done. Uterus appeared normal. Left side ovary appeared normal size and structure with intact capsule. Biopsy was taken and tissue was sent for frozen section which revealed normal histology and no areas of neoplastic change. Left fallopian tube was normal. Figure 7 shows adnexa preserved on the left side. Bilateral pelvic regions were examined, no lymph nodes were found to be involved. No para- aortic lymph nodes were palpable.

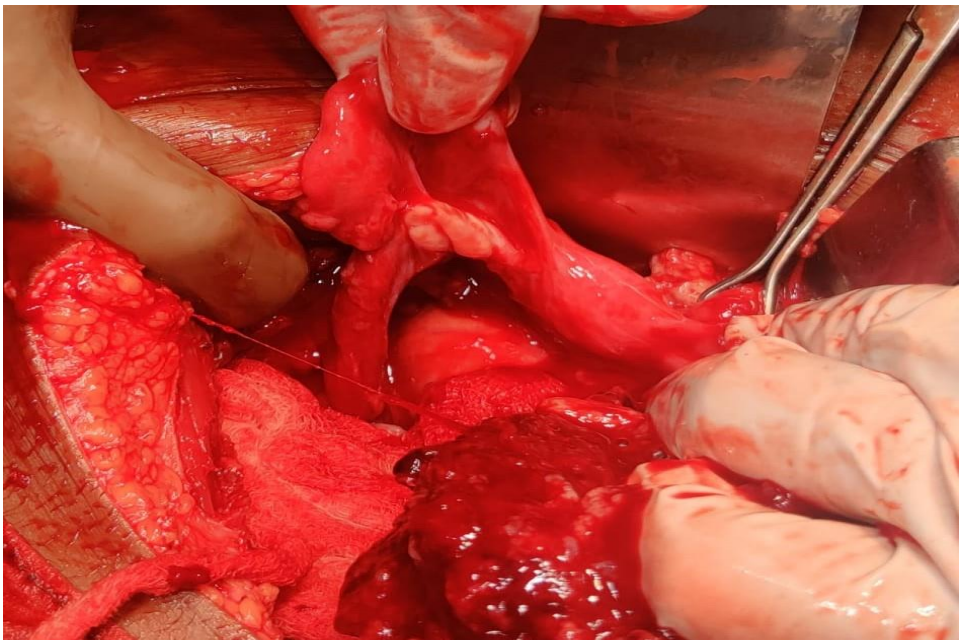

Figure 7 Adnexa preserved on the left side

HPE report

On gross examination, the mass weighed 2.5 kgs and measured 25 x 17x 14 cms. It was friable irregular yellowish- white mass. The cut surface showed multiple yellowish variegated spaces of necrosis and haemorrhage. There were numerous yellowish cheesy areas and cystic spaces which were filled with straw coloured clear fluid. On microscopic examination, sections revealed broad areas of solid grey-white homogenous areas which were consistent with mixed germ cell tumour of ovary (Dysgerminoma and yolk sac). Cells have hyperchromatic nucleus showing pleomorphism with prominent nucleoli. Cell block study of ascitic fluid was suggestive of leucocytic exudation (figure 8 and 9). There was no evidence of malignant cells in omental biopsy and ascitic fluid.TNM staging: pT3CpNXpM1 (Stage IV)

Patient's intra-op findings along with HPE report was discussed with MDT in Institutional Tumour Board and plan given was chemotherapy consisting of BEP (Bleomycin, Etoposide and Platinum) 3 weekly for 4 cycles. Patient was advised for regular follow up with serum tumour markers (LDH, Beta HCG and AFP) along with USG before every cycle and thereafter 3 monthly for 1 year and then every 6 months for next 2 years.

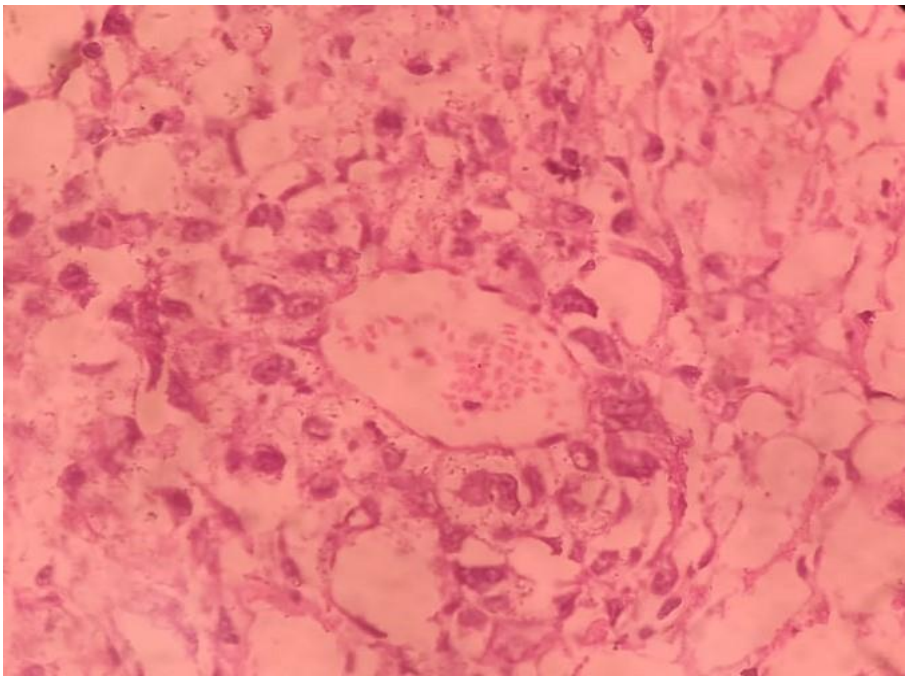

Figure 8 Photomicrograph showing Schiller Duval body

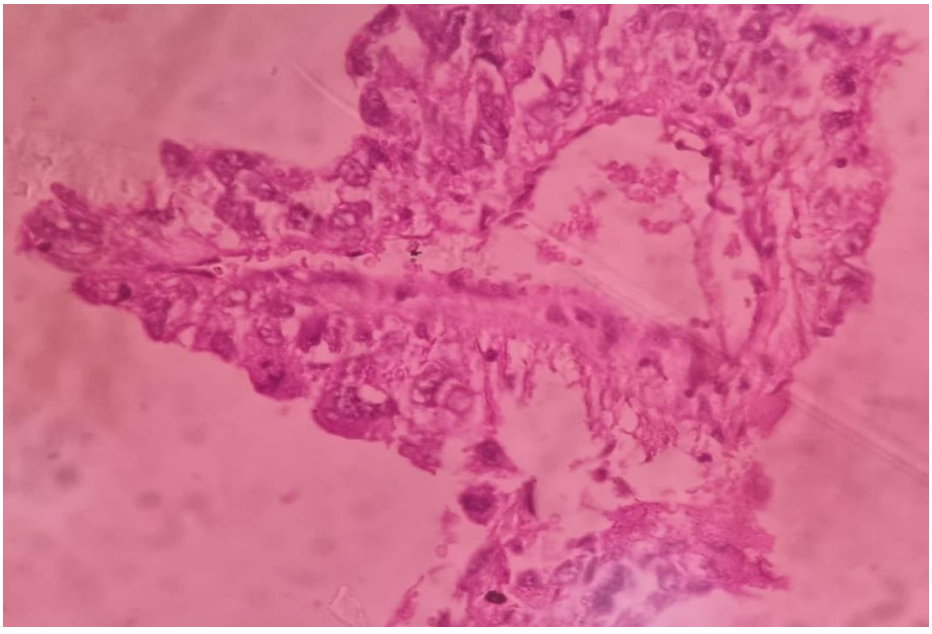

Figure 9 Photomicrograph showing component of dysgerminoma

3. DISCUSSION

Ovarian neoplasms contribute to around 2% of tumours among adolescent age group (Quddusi et al., 2013). In adolescents, malignant ovarian tumours are generally suspected when patient presents with symptoms and are diagnosed while performing physical examination. They are at times discovered as incidental findings through radiological imaging. The ability to diagnose accurately at an initial stage and able to preserve fertility are of utmost value in patients of adolescent age group. Recent studies have reported that among adolescents who have underwent surgery for persistent ovarian tumours; the rate of malignancy is found to be around 5%-9% (Reddy & Laufer, 2009).

Though gynaecological neoplasms are relatively rare in adolescent age group, they should still be considered with utmost vigilance when an adolescent presents with complaints of discomfort or lump in abdomen. The most common presenting symptoms could be mass abdomen associated with distension excruciating pain in abdomen, abnormal menstrual complaints or other bowel or bladder related symptoms. The mainstay in management of an adolescent ovarian neoplasm is largely similar to that of an adult ovarian neoplasm but for the major difference being preservation of the anatomy as much as possible in order to retain the reproductive ability (Quddusi et al., 2013). In every case, extreme care has to be taken while handling tissue, during haemostasis and all the steps to prevent adhesions are to be followed meticulously so that the fertility of the patient is preserved. Frozen section must be performed as it helps in confirming the diagnosis. The possibilities of a pelvic mass to be functional are high in an adolescent who has already attained menarche (Berek et al., 2013).

Germ cell tumours are classified as Endodermal sinus tumour (Yolk sac tumour), Dysgerminoma, Polyembryoma, non-gestational Choriocarcinoma, Embryonal carcinoma, Teratomas (Mature, Immature and Mono-dermal), Gonadoblastoma and Mixed. Presenting a case of malignant mixed germ cell tumour consisting of two major components that of yolk sac tumour and dysgerminoma. This rare combination in literature accounts for about 1/3rd of all cases (Gershenson, 1993) other combinations being immature teratoma and choriocarcinoma in their increasing trend of frequency. The endodermal sinus tumours or the yolk sac tumours take their origin from primitive yolk sac. On gross examination, they are soft grey-brown lesions comprising of cystic spaces which are formed due to degeneration or necrosis. These lesions proliferate rapidly. On Microscopic examination, the characteristic feature is Schiller- Duval body or endodermal sinus. Fig.8 Photomicrograph showing Schiller Duval body. Most of the yolk sac tumours generally secrete AFP (alpha fetoprotein) and rarely alpha-1 antitrypsin. Though they are extremely aggressive tumours, the five-year survival rate of stage 1 tumours was found to be around 92 % when effectively managed with surgery followed by chemotherapy. While the rate of survival in more advanced disease was found to be 29% to 44% respectively (Kawai et al., 1991).

Dysgerminoma being the most common malignant germ cell tumour accounts for 30-40% of all ovarian neoplasms of germ cell origin. The size of dysgerminoma varies widely, but are usually around 5-15 cms in diameter. The capsule is slightly bosselated and on cut surface, it is pale tan to grey-brown in colour with fleshy consistency. The histologic characteristics of dysgerminoma are polygonal or ovoid cells having abundant pale cytoplasm. Fig. 9 Photomicrograph showing component of dysgerminoma.One of the significant features of dysgerminoma is that it is the only germ cell malignancy which has bilaterality.

In our case, an adolescent girl presented with rapidly growing huge mass in the abdomen extending above the umbilicus with abnormally raised levels of AFP and LDH which lead to the suspicion of malignant mixed germ cell tumour comprising of yolk sac tumour and dysgerminoma. Presence of a massive, unilateral bosselated mass on laparotomy followed by histopathological examination confirmed the diagnosis of mixed malignant germ cell tumour. Presence of mixed germ cell tumour with a combination of yolk sac tumour and dysgerminoma is quite rare with very few reported cases. Such lesions in adolescents should be best managed by complete cyto-reductive surgery (considering fertility preservation) followed by neo-adjuvant chemotherapy, with preferred combination of BEP (Bleomycin, Etoposide and Platinum). With the advancements in recent technologies, with conservative surgery and combination chemotherapy, the survival rate among early and advanced stage tumours have been drastically improved to 98% and 94% respectively (Low et al., 2001).

Nishio et al., (2006) has demonstrated that among patients with malignant germ cell tumours of the ovary, at any clinical stage the kind of surgical procedure performed was not considered an important prognostic factor. It indicates that conservative surgery (fertility preserving) is considered appropriate as far as chemotherapeutic agents are being employed effectively (Tewari et al., 2000). The serum markers though positive initially might become negative following chemotherapy, but this observation may indicate regression of only a specific component of the mixed lesion. The size of the primary tumour is considered to be the most significant prognostic feature followed by relative size of the most malignant component. Although, most of the patients suffering from malignant mixed ovarian germ cell tumours are managed effectively, a few of them might develop recurrence usually within 2

years of primary diagnosis. Since relapse is rare among this population, there has been no standard approach, with management strategies extrapolated from clinical experience among testicular cancer patients (Gershenson, 2007).

4. CONCLUSION

Malignant mixed germ cell tumour (yolk sac tumour and dysgerminoma) is an extremely uncommon and highly malignant ovarian tumour. A meticulously performed surgery followed by adequate staging biopsies and combination chemotherapy can massively improve the prognosis of these patients.

Acknowledgement

We would like to thank all the participants for the constant efforts and sincere contribution towards the study.

Author Contribution

Dr. A Manisha has collected information and prepared the manuscript which has been thoroughly reviewed by Dr. Deepika Deewani and Dr. Kalyani Mahajan. Dr. Subhada Jajoo madam has further added her valuable inputs. Dr. Srinidhi Cherukuri has helped in further modification of the manuscript.

Informed Consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Funding

This study has not received any external funding.

Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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