MÆDICA - a Journal of Clinical Medicine

CASE REPORT

MAEDICA – a Journal of Clinical Medicine
2024; 19(3): 662-666
https://doi.org/10.26574/maedica.2024.19.3.662

Mixed Germ Cell Tumor (GCT) of Ovary with Atypical Presentation

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ABSTRACT

Objective: *Ovarian carcinomas are considered one of the deadliest malignancies, accounting for a significant number of cancer-related deaths than any other gynaecological malignancy. Advanced stage at diagnosis can be attributed to vague presenting symptoms, rarely bizarre, which usually point towards any disease but ovarian tumour. Here, we discuss a similar case, with presentations that compels us to think in favor of disseminated Koch's, but turns out to be germ cell tumor (GCT) of the ovary; thereby pointing at the wide spectrum of bizarre signs and symptoms which should have ovarian malignancies as a differential during workup.*

Case report: *A 21-year-old unmarried female came to our gynaecology outpatient department with complaints of pain lower abdomen, high-grade fever, shortness of breath and progressively increasing abdominal distension. After routine hematological and imaging workup, she was diagnosed with an ovarian tumour with ascites and bilateral pleural effusion. Fertility-sparing surgery was done after the patient was hemodynamically stable. The histopathology report was suggestive of mixed GCT. The patient was thereby referred to the department of medical oncology for adjuvant chemotherapy.*

Conclusion: *Mixed GCTs are among the rare and inordinately malignant tumours of the ovary. Though they have their usual presentations, we ought to be heedful of their atypical presentations as well because these form grounds for early diagnosis and management. In our patients, the unusual feature was the high-grade fever with associated shortness of breath (due to pleural effusion), but the effusion was non-malignant and non-infectious in origin. In the literature there are not many cases of atypical clinical presentation; hence, this could be an area of further research. Besides, such case reports with bizarre manifestations widen our spectrum of diagnostic probabilities, thereby avoiding any gaps in management. Our workup should be comprehensive enough to diagnose the patient as early as possible because these tumors, though aggressive, have a very good prognosis due to excellent chemosensitivity.*

Keywords: disseminated Koch's, chemosensitivity, fertility-sparing surgery, erm cell tumour, high-grade fever.

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Article received on the 3rd of July 2024 and accepted for publication on the 26th of September 2024

INTRODUCTION

Worldwide, ovarian cancer accounts for 225,000 new cases and 140,000 deaths every year (1). Ovarian cancer accounts for 5% of all malignancies and 25% of female genital tract-related malignancies (2). It is the third most common cancer among Indian women after cervical cancer and breast cancer. Based on the anatomical structures from which the tumours originate, ovarian cancers have been classified as epithelial ovarian cancers (EOC) (90-95%), germ cell tumours (GCT) and sex cord stromal tumours (SCST) (5-10% combinedly). Germ cell tumor originates from primitive germ cells of the ovary, with 95% of GCTs being benign and 2-3% malignant (3).

Patients with malignant ovarian masses, especially GCT, typically present with subacute abdominal pain (85%), acute abdomen (due to torsion, rupture) in 10% of cases, while the remaining 5% of patients can have variable presentations (3).

Here, we report a case of ovarian GCT with such deviant presentation in the form of high-grade fever with shortness of breath in association with pain abdomen and distension per abdomen, which usually is a feature of advanced-stage disease. ❑

CASE PRESENTATION

A 21-year-old unmarried female visited our gynaecology outpatient department with chief complaints of pain in the lower abdomen for 15 days, fever for 10 days and abdominal distension for seven days. She was apparently well 15 days back, when she developed pain in the lower abdomen, which was insidious in onset, non-radiating, intermittent, dull-aching, no aggravating factor and relieved by medications, but increased in severity over next l0 days. It was followed by high-grade fever associated with chills and rigors. Fever was accompanied by cough without expectoration, followed by increasing abdominal distension for seven days coupled with decreased appetite, though there was no history of weight loss or night sweats. The patient also complained of shortness of breath on exertion for four days, which was not associated with any chest pain, palpitations, or swelling of feet. There was no family history of any breast, endometrial, ovarian, or gastrointestinal malignancies. The patient visited a private hospital with the above complaints; ascitic tap was done and she was started on anti-tubercular treatment (ATT) after ascitic fluid cytology (reports not available).

On examination, her general condition was fair and pallor was present. Her blood pressure was within normal limits, but she had tachycardia with tachypnoea. On chest auscultation, bilateral air entry was decreased without any adventitious sounds. On *per* abdominal examination, the abdomen was distended and a vague ill-defined mass, firm in consistency and with restricted mobility could be palpated with difficulty in the hypogastrium. The patient visited our institute with the described complaints and she

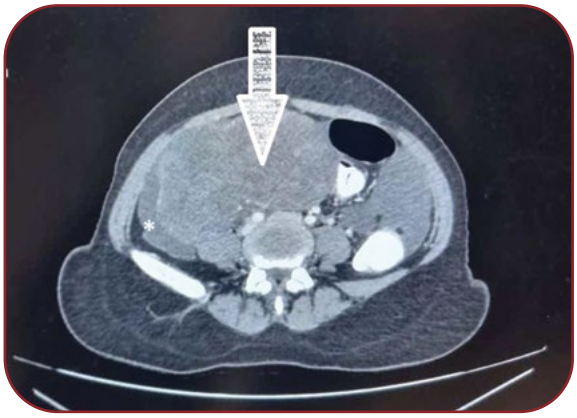

FIGURE 1. Contrast enhanced computed tomography scan abdomen (axial view) showing solid nodular ovarian mass (white arrow) and ascites (asterisk)

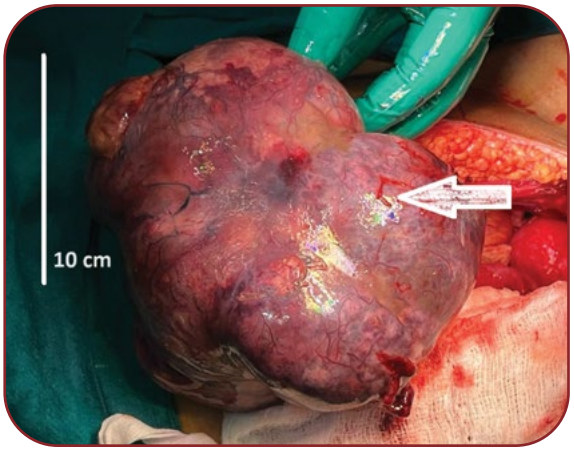

FIGURE 2. Intraoperative image showing a lobulated, irregular and congested mass of 14.5x14x8.5 cm in the right ovary mass (white arrow)

TABLE 1. Summary of blood and imaging investigations

Subject No.	Parameters	Results
1.	Haemoglobin TLC Platelets	6.1 gm/dL 13,390 cells/cumm 7.0 lakh/cumm
2.	Dengue (NS1 Ag/IgM) Widal Malaria	Negative <1:20 titre for O, H, AH antigen Negative
3.	CA-125 CA 19-9 β HCG α-fetoprotein LDH CEA	135 U/mL 126 U/mL 567.83 ng/mL 1313 ng/mL 1367 U/L 1.03 ng/mL
4.	KFT Blood urea Serum creatinine Uric acid	 22 mg/dL 0.98 mg/dL 3.3 mg/dL
5.	LFT SGOT/SGPT ALP Total protein/albumin/globulin Total bilirubin/direct bilirubin	 39.3/9.6 U/L 26 U/L 0.64/0.22/0.42 g/dL 7.2/2.7 mg/dL
6.	Serum Na^+/serum K^+	140/4.71 mEq/L
7.	Serum Ca^{++}	6.33 mg/dL
8.	High sensitive CRP	191.68 mg/dL (lab range <1 mg/dL)
7.	Blood culture/urine culture	No growth
8.	Ascitic fluid biochemistry Glucose Protein	77 4.97 2.40
9.	Ascitic/pleural fluid cytology	Negative for malignancy and tuberculosis
10.	USG (pelvis)	Heterogenous mass seen arising from right adnexa, showing solid-cystic component, internal vascularity – likely right ovarian mass. Uterus and left ovary – normal. Moderate ascites detected.
11.	CECT abdomen	Heterogeneously enhancing abdominopelvic mass of 12.3x6.8x12 cm in the right adnexal region with solid-cystic component, compressing and encircling right ureter at the level of crossing with ileal vessels with associated mild hydroureteronephrosis. No overt invasion of the ureter was seen. Significant increased omental vascularity and nodularity seen. High-density ascites (high proteinaceous/blood stained), no overt liver surface deposits. Few centimetric para-aortic lymph nodes seen at the renal level.
12.	CECT thorax	Moderate left pleural effusion with pleural separation of approximately 4.5 cm and underlying subsegmental atelectatic changes. Minimal right pleural effusion with a thin atelectatic band in the right lower lobe. Rest of the lung parenchyma normal bilaterally.

was admitted for further evaluation and management. Relevant blood biochemistry and imaging studies were done (Table 1).

Diagnostic ascitic and pleural tapping were found negative for tuberculosis. Two units of packed red cells were transfused given severe anemia. Based on history and examination, our first differential was abdominal tuberculosis. However, the imaging studies established the diagnosis of ovarian mass with an increased probability of GCT of the ovary (increased β-HCG, α-fetoprotein levels and young age). Though we suspected tumor lysis syndrome, neither the laboratory nor clinical criteria were met.

The case was discussed in the tumour board. The patient was eventually planned for exploratory laparotomy, followed by fertility-sparing debulking surgery after eight days of admission once she was hemodynamically stable. Intraoperatively, golden brown ascitic fluid was seen, which was sent for cytology to check the presence of malignancy. A 14.5x14x8.5 cm lobulated, irregular, congested mass arising from the right ovary, with capsule breached at two places approximately 3.5x1.5 cm and 1.5x1.3 cm – surgical stage IC2 (FIGO 2014) – was identified. Clockwise exploration of abdominal organs was done – no gross tumour deposits were found. Right salpingo-oophorectomy was done. Bowel

and omentum oedematous and adherent to each other and the anterior abdominal wall above umbilicus; infracolic omentectomy was done, and peritoneal biopsy was taken from bilateral paracolic gutters and bladder peritoneum. Right-sided retroperitoneal lymph node dissection was performed as a few centimetric paraaortic lymph nodes were seen on contrast enhanced computed tomography (CT) scan. On histopathology, it was a mixed germ cell tumour with components of embryonal cell carcinoma (5%) and yolk sac tumour (95%), weighing 964.5 grams; all remaining tissues were confirmed to be free of tumour. The postoperative period was uneventful and the patient was discharged on the 10th day after surgery in satisfactory condition, with advice to follow up in medical oncology also for adjuvant chemotherapy. The patient was planned for BEP (Bleomycin + Etoposide + Cisplatin) regimen and is currently receiving it. She will be followed up after chemotherapy for another five years for disease recurrence and overall survival. ❑

DISCUSSION

Malignant germ cell tumours of the ovary form a trifling spectrum of gynaecological malignancies. They are further classified into subtypes based on histologic features and immunohistochemical expression of tumour markers. Dysgerminomas are among the most common subtypes of GCT, followed by immature teratomas and yolk sac tumour.

A mixed GCT is a relatively scarce tumor consisting of two or more germ cell components. Embryonal cell carcinoma and mixed GCT are among the rare GCTs of the ovary. Amongst mixed GCT, dysgerminoma is the most frequent component (80%), followed by yolk sac tumour (70%), immature teratoma (53%), choriocarcinoma (20%) and embryonal carcinoma (16%). In the literature, dysgerminoma and yolk sac tumor is the most commonly reported combination which makes one third of the total cases of mixed GCTs. The distinguishing features of GCT are younger age at presentation (usually teens or early 20s), most often stage I at diagnosis, and excellent prognosis due to impeccable tumour chemosensitivity. The preferred chemotherapy regimen is BEP (3-6).

In these patients, presenting symptoms usually comprise lower abdominal pain, distention or mass per abdomen. Acute symptoms due to tumor torsion, rupture or hemorrhage are seen in approximately 10% of patients (7, 8).

Diagnostic workup *as per* the European Society for Medical Oncology (ESMO) clinical practice guidelines includes chest X-ray, pelvic ultrasound, abdominopelvic CT scan and positron emission tomography scan in selected cases of ovarian GCTs (9). Preoperative evaluation should include serum β-hCG, α-fetoprotein, LDH and CA-125 levels in young patients. The current Royal College of Obstetricians and Gynaecologists (RCOG) guideline for ovarian mass in premenopausal women recommends the determination of serum LDH, AFP and βhCG levels in all women under 40 years. The National Academy of Clinical Biochemistry guideline recommends that AFP and βhCG levels should be measured whenever there is suspicion of GCT in women younger than 40 years. Regression of tumor marker is a good predictor of prognosis (10).

Fertility preservation is an important component in managing the GCT of the ovary as patients are usually young females, mostly unmarried or nulligravid. Primary debulking is the cardinal step due to early stage at diagnosis and reduced tumour load after surgery; the latter is favorable for encouraging chemotherapy results. Besides, patients can have normal menses and subsequent pregnancies following the completion of treatment and follow-up. The standard treatment protocol includes unilateral adnexectomy, omentectomy, peritoneal washings, peritoneal biopsies and retroperitoneal lymph node dissection, followed by adjuvant chemotherapy, as these tumors are highly chemosensitive. There are a number of studies supporting the safety of unilateral oophorectomy in non-malignant germ cell tumors (11, 12).

Factors determining prognosis include the size of the primary tumour and the percentage of corresponding malignant integrant. Tumours with surgical stage IA and size less than 10 cm have 100% survival. Tumours with one component as yolk sac tumour or choriocarcinoma, or immature teratoma (grade 3) forming less than one third of the whole tumour, also have an excellent prognosis. In the remaining cases, prognosis is less favorable. ❑

CONCLUSION

Mixed GCTs are among the rare and inordinately malignant tumours of the ovary. Though they have their usual presentations, we ought to be heedful of their bizarre presentations because they are grounds for early diagnosis and management. In our patient, the unusual feature was high-grade fever with associated shortness of breath (due to pleural effusion), but the effusion was non-malignant and non-infectious in origin. In the literature there are not many cases of atypical clinical presentation; hence, this could be an area of further research. Besides, such case reports with bizarre manifestations widen our spectrum of diagnostic probabilities, thereby avoiding any gaps in management. ❑

Conflicts of interest: none declared.

Financial support: none declared.

Informed consent was obtained from the patient regarding using her data for medical studies.

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