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Case Report

Non-gestational choriocarcinoma of the ovary: A case report

Loh S. Yee, MD [a], Rosnani Zakaria, FRACGP [a,*], Noraini Mohamad, MMED [b] and Ong W. Fong, MD [c]

[a] *Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Malaysia*
[b] *Department of Medicine, School of Dental Sciences, Universiti Sains Malaysia, Kubang Kerian, Malaysia*
[c] *Department of Radiology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Malaysia*

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الملخص

إن سرطانة المبيض المشيمائية غير الحملية هي حالة سريرية نادرة للغاية. وهناك عدد قليل جدا من الحالات عالية الخباثة تم الإبلاغ عنها في الأدبيات في جميع أنحاء العالم. نظرا لندرة الورم، يتم تجاهل هذا المرض بشكل عام، مما يؤدي إلى تأخر التشخيص والعلاج. بالنسبة للأطباء المختصين، تشكل سرطانة المبيض المشيمائية غير الحملية تحديا تشخيصيا بسبب أعراضها السريرية غير المحددة. نقدم حالة فتاة تبلغ من العمر ١٦ عاما راجعت بألم في الحفرة الحرقفية اليمنى واختبار بول للحمل إيجابي. على الرغم من كونها غير نشطة جنسيا، تم تشخيص المريضة بحمل خارج الرحم وخضعت لعملية إسعافية جراحية بالمنظار. بعد ستة أسابيع، أظهر التحليل الهستوولوجي تشخيص سرطانة المبيض المشيمائية غير الحملية. وأظهرت تقييمات أخرى أن سرطانها قد تقدم بالفعل إلى المرحلة الرابعة. في هذا التقرير، يتم مناقشة الأعراض غير المحددة للمرض، والسمات الإشعاعية، والعلاجات الحالية واستراتيجيات السلامة الممكنة.

الكلمات المفتاحية: المراهقة؛ سرطانة المشيمائية؛ الحمل خارج الرحم؛ سرطانة المبيض المشيمائية غير الحملية؛ الأورام المبيضية

Abstract

Non-gestational choriocarcinoma of the ovary is an extremely rare clinical condition. Very few cases of this high-grade malignancy of the ovary are reported in the literature worldwide. Given the rarity of the tumour, this disease is generally overlooked, which leads to delayed diagnosis and management. For the attending clinicians, the non-gestational choriocarcinoma of the ovary poses a diagnostic challenge due to its non-specific clinical presentations. A 16-year-old girl presented with pain in the right iliac fossa and with a positive urine pregnancy test. Despite being sexually inactive, the patient was diagnosed with an ectopic pregnancy and underwent emergency laparoscopic surgery. Six weeks later, the histopathological analysis revealed a diagnosis of non-gestational choriocarcinoma of the ovary. Further evaluations showed that her cancer had already advanced to stage IV. In this case report, the non-specific presentations of the disease, radiological features, current treatments, and possible safety strategies are discussed.

Keywords: Adolescent; Choriocarcinoma; Ectopic pregnancy; Non-gestational choriocarcinoma; Ovarian neoplasms

Introduction

Ovarian cancer is the third most common gynaecologic cancer after cervical and uterine cancer.[1] Among women, ovarian cancer accounts for around 4% of cancer incidence and mortality worldwide.[1] In Malaysia, the percentage for incidence and mortality of ovarian cancer in 2018 were 2.9% and 3.0%, respectively.[2]

Choriocarcinoma is a highly malignant tumour with trophoblastic differentiation. Choriocarcinoma arising in the ovary is a rare malignant condition and can be classified as gestational or non-gestational in origin and can be a primary

* Corresponding address: Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, 16150, Kubang Kerian, Malaysia
E-mail: rosnaniz74@gmail.com (R. Zakaria)
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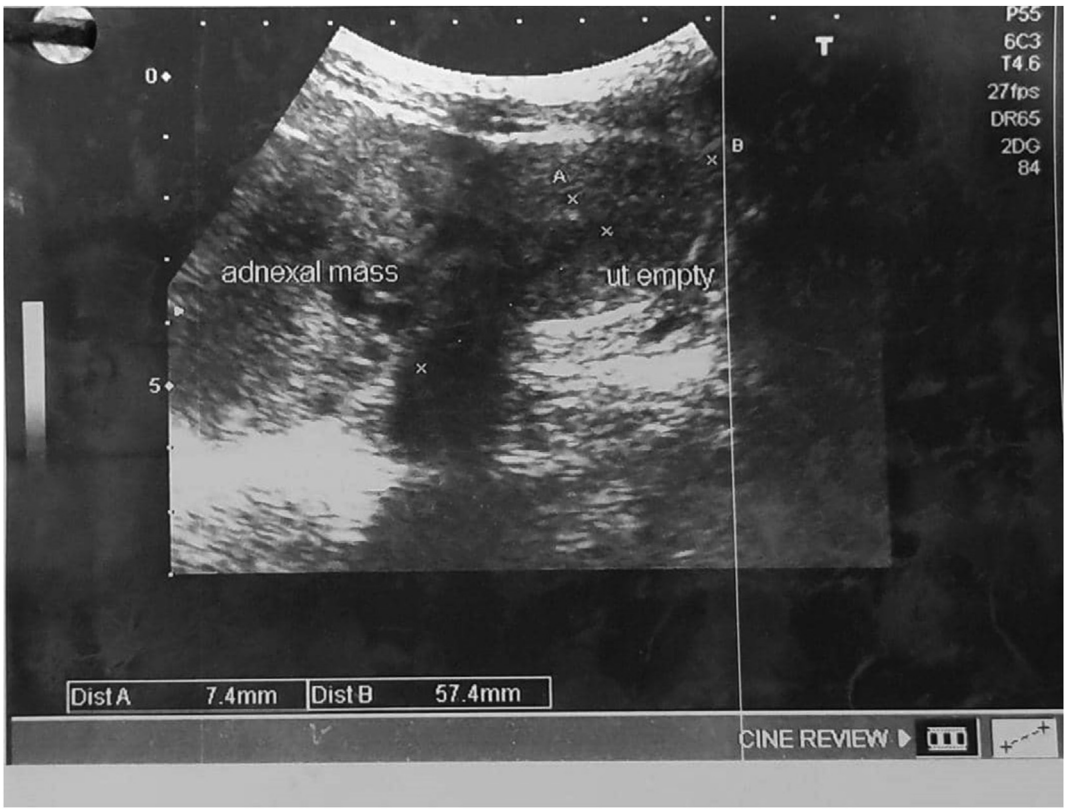

Figure 1: Right adnexal mass of 6.25 cm × 5.96 cm and empty uterus.

tumour or metastatic from other organs.[3] Epidemiologically, the gestational type is more common than the non-gestational type, and only a few cases of non-gestational choriocarcinoma of the ovary (NGCO) have been reported in the literature worldwide.[4] Generally, NGCO have been clinically diagnosed in female patients who were sexually immature, unable to conceive, or have never had sexual intercourse.[5] Ovarian germ cell tumours commonly occur in the first two decades of life, but can also be seen in any age group.[6]

NGCO has poor prognosis, hence, early diagnosis and timely initiation of chemotherapy are important. However, due to non-specific symptoms of the disease, it may be easily misdiagnosed, leading to delayed treatment. Therefore, high level of clinical suspicion is pivotal to avoid missing the diagnosis of such disease.

Case report

A 16-year-old girl presented to a general practitioner with the complaint of right lower abdominal pain of one day duration. She experienced tenderness on palpation at the right iliac fossa region with rebound tenderness. The doctor suspected acute appendicitis and immediately referred her to the nearest district hospital.

At the district hospital, the girl's condition was assessed and detailed history was taken. There was no vaginal bleeding and her last menstrual period was eight days ago. She denied any fever or urinary symptoms. There were no loss of appetite, nausea, or vomiting. She is single and strongly denied any history of sexual activity. She has no significant past medical and surgical history and no family history of malignancy. She did not have any drug or food allergies. She attained menarche at the age of 14 years and her menses were regular. She is a student from secondary school and denied ever having a boyfriend.

Clinically, she is alert, conscious, not pale, and her physical examination showed that her vital signs were normal. The abdomen was mildly tender and there was a vague mass palpable over the right lower quadrant. There was no hepatosplenomegaly, no ascites and no palpable lymph node. Other systemic examinations were unremarkable. Transabdominal ultrasound revealed a right adnexal mass of 6.25 × 5.96 centimetre (cm) and an empty uterus (Figure 1). Subsequently, permission to conduct urine pregnancy test (UPT) was obtained from the patient and her mother. The UPT done by using urine dipstick was positive. Repeated UPT using both urine dipstick and sample collection for laboratory analysis were done as patient persistently denied any sexual activity, but the result remained the same. Hence, she was diagnosed with a case of ectopic pregnancy.

She underwent an emergency laparoscopic left cystectomy with partial left oophorectomy. Intraoperatively, the left ovary was haemorrhagic with friable tissue and with minimal hemoperitoneum. There was no product of conception. The left ovarian tissue was sent for histopathological examination. At this stage, the diagnosis given was left ovarian ectopic. Thus, UPT was not repeated and serum beta-human

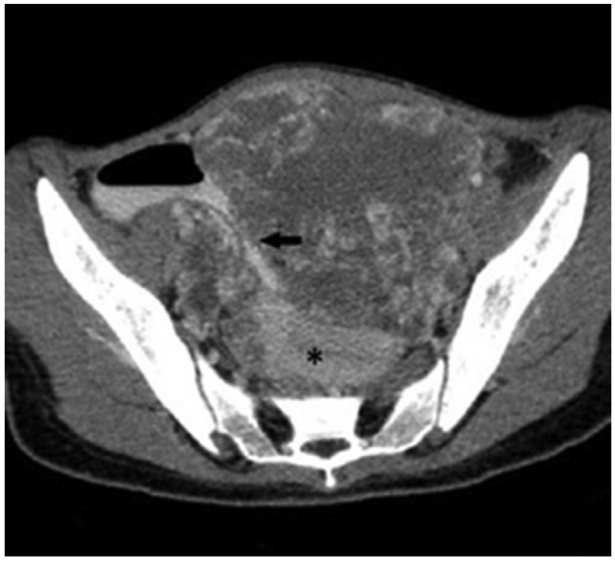

Figure 2: Multiloculated cystic mass with high vascularity within the pelvis displacing the uterus (asterisk) posteriorly and compressing onto the adjacent small bowel loops (arrow). Largest dimension of mass is 9.5 cm × 12.0 cm × 11.1 cm.

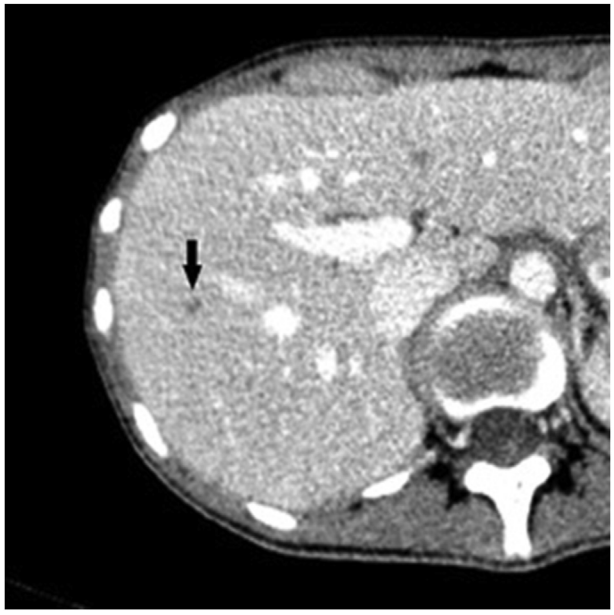

Figure 4: Ill-defined hypodense lesion (arrow) in segment V of the liver which is suspicious of liver metastasis.

chorionic gonadotropin was not taken post-operatively. There were no post-operative complications and she was discharged three days after surgery. She was given a routine follow-up date in six weeks at the gynaecology clinic to review her condition and histopathological result. No other advice was given.

Upon follow-up, she looked thinner and she reported loss of appetite and had lost four kilograms (kg) in weight post-operatively. The family thought it was due to the trauma of the surgery. However, the histopathological result revealed she had NGCO. This explained the reason for persistent positive UPTs before.

Subsequently, blood investigations were taken, and arrangements were made to perform a computed tomography scan. Both her serum beta-human chorionic gonadotropin (beta-HCG) and cancer antigen 125 (CA-125) were elevated with a value of 624,177 milli-international units per millilitre (mIU/mL) and 151.6 units per millilitre (U/mL), respectively. Other tumour markers such as carcinoembryonic antigen (CEA) and alpha fetal protein were within the normal range. Computed tomography of the thorax, abdomen, and pelvis demonstrated bilateral multiloculated, heterogenous lesion with high vascularity suggestive of ovarian lesion and highly indicative of carcinoma (Figure 2). There was a solitary lung nodule seen at the middle lobe (Figure 3) and there was presence of an ill-defined hypodense liver lesion, suggesting metastasis (Figure 4). Based on the histological and imaging findings, she was diagnosed with NGCO with lung and liver metastases (Stage 4).

Therefore, she was referred to oncologist at the tertiary hospital for further management. Unfortunately, she developed persistent anaemia secondary to bleeding tumour and required multiple blood transfusions. Post optimisation of her condition and blood parameters, the team started her on BEP regime (bleomycin, etoposide, and cisplatin). The BEP regimen consisted of 15 units bleomycin, 100 milligram per square meter (mg/m^2) etoposide and 20 mg/m^2 cisplatin. However, due to the advanced stage of her cancer, she developed one complication after another. She had left pleural effusion and multiple hypotensive episodes and respiratory failure despite optimal treatment efforts. She eventually ends up with multiple organ failure and succumbed to her illness within one month of admission.

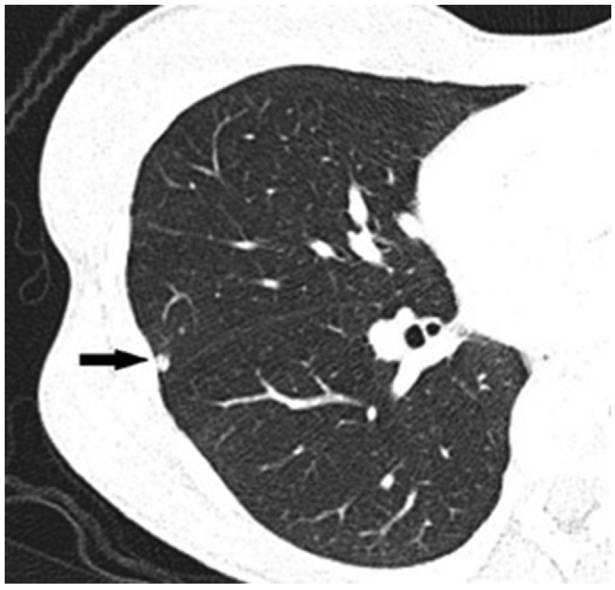

Figure 3: Solid round lung nodule in the lateral segment of the right middle lobe in keeping with lung metastasis.

Discussion

Choriocarcinoma can be either gestational or non-gestational type. Gestational choriocarcinoma of the ovary may arise from an ovarian pregnancy or as a metastatic choriocarcinoma from a primary gestational choriocarcinoma arising in other parts of the genital tract, while non-gestational type arises as a germ cell tumour with differentiation into trophoblastic structures.[7]

NGCO is an extremely rare malignant germ cell tumour with incidence of less than 1% of all ovarian germ cell tumours, nonetheless it is prevalent among women of reproductive age especially adolescents.[4] The clinical symptoms of the disease are normally non-specific and may include abdominal pain and vaginal bleeding.[8] These symptoms mimic the presentations of other more common conditions occurring in young women, such as tubo-ovarian abscess and ectopic pregnancy.[3]

Therefore, misdiagnosis is very high, as in this case, symptoms, clinical signs, and ultrasonographic findings, led to the diagnosis of ectopic pregnancy. The diagnosis is usually established post-operatively, after histopathological examination of the removed ovarian tumour.[8]

The tumour is composed of two cell lines of cytotrophoblast and syncytiotrophoblast that secrete beta-HCG.[9] This explains the positive UPT results with the absence of pregnancy. The tumour has a high tendency to metastasise early via hematogenous dissemination, to the lung (80%), pelvis (20%), liver (10%), and other rare sites including gastrointestinal tract, spleen, and kidney.[9] For this reason, to solely assume pregnancy due to the positive UPT results in women of reproductive age with no history of sexual activity is discouraged.

Our patient strongly denied any experience of sexual intercourse, and clinicians should be more accepting and investigate further for the possibility of something sinister, such as a malignancy, especially after laparoscopic finding of no product of conception.[10]

Serum beta-HCG should be tested in young women with pelvic masses demonstrated on ultrasonographic findings.[11] Jiao et al. reported that serial measurement of beta-HCG level is crucial for early diagnosis of NGCO, particularly in those pubertal females with ovarian mass.[12] In this case, if serial serum beta-HCG was done and the level was monitored regularly, the trend may alert the possibility of NGCO and proactive management will be carried out.

Post-operative advice for warning signs to look for such as significant weight lost, was not given, this safety netting advice may prompt the patient and parents to seek medical advice sooner and the matter will be identified sooner.[13]

In this case, delay in obtaining an accurate diagnosis resulted in a more loco-regionally advanced disease. The patient was diagnosed with NGCO stage 4, with evidence of pulmonary and liver metastasis.

Irene et al. reported that although NGCO has a poorer diagnosis, there are numerous cases of complete resolution of symptoms.[7] In Japan, Hayashi et al., reported a 10-year girl with NGCO survived the disease and was disease free up to 62-months follow-up. She was diagnosed early and received chemotherapy a week post surgery.[14] Early diagnosis and multi-agent chemotherapy are affiliated with high cure rates.[6] Therefore, prompt diagnosis and early initiation of therapy are important factors for a better prognosis.

Conclusion

In conclusion, NGCO is a rare cancer however, despite its rarity, it must be considered as one of the differential diagnosis in women with adnexal mass and increased serum beta-HCG. Early detection and appropriate management may improve the patient's outcome.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

We have made the effort to remove any possible clues of identifying the patient. There is no ethical issue in this case report as to our knowledge.

Consent

During the research activities, Our patient unfortunately passed away in 2019 as was stated in the case report. We got her parents consent for her case to be published.

Authors contributions

SYL conceived the idea, wrote the initial draft and provided logistic support. RZ supervised, reviewed, edited, and wrote the final draft. NM supervised, reviewed, and edited the draft. WFO provided resources and visualisation of the images. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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