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# A successful spontaneous pregnancy after surgery and chemotherapy in a patient with recurrent dysgerminoma: A case report

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**Abstract:**

Dysgerminoma comprises 3%–5% among ovarian malignancies, mostly seen in adolescent and early adult women. The recurrence rate is approximately 10%–20%, occurring within 2 years of diagnosis, and has been reported that more than 75% occur in the 1st year. A 19-year-old nulligravid initially presented with severe abdominal pain, who underwent emergency exploratory laparotomy and left salpingo-oophorectomy, whose histopathologic result revealed dysgerminoma, Stage IC2. Recurrence of dysgerminoma was noted on the contralateral ovary 10 months after for which she had undergone another surgery for wedge resection of the right ovarian mass and complete surgical staging. She received adjuvant chemotherapy without complications. Despite two consecutive surgeries and chemotherapy, she had conceived naturally and her pregnancy was carried to term with no complications and delivered to a live baby girl by normal spontaneous delivery. This case is a proof of how fertility-sparing surgeries and chemotherapy in dysgerminoma can successfully preserve reproductive functions for future conceptions.

**Keywords:**

Adjuvant chemotherapy, dysgerminoma, pregnancy, recurrence

## Introduction

Dysgerminoma is a malignant ovarian germ cell tumor (MOGCT), which may occur at any age, but is mostly seen in adolescents and early adulthood. It is the most common germ cell tumor, accounting for 1%–2% of primary ovarian neoplasms.[1] Most patients present with a unilateral ovarian mass in 85%.[1] Occurrence of relapse usually happens within 2 years of diagnosis, with a recurrence rate of approximately 10%–20%, of which more than 75% occur in the 1st year.[1] In general, for young patients, unilateral salpingo-oophorectomy (USO) with complete surgical staging is the primary treatment, with or without tumor debulking and adjuvant chemotherapy, depending on the stage.[2] This aims to preserve fertility while ensuring that no recurrence would ensue. Here, we present a case of a young patient who had a successful natural pregnancy after incurring a recurrent dysgerminoma managed with wedge resection of recurrent dysgerminoma and adjuvant chemotherapy.

## Case Report

A 19-year-old female, nulligravid, was initially managed as a case of left ovarian new growth probably twisted due to the presence of severe abdominal pain. Her past medical and family medical history was noncontributory. She noted regular menses occurring every month, and no

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sexual contact at this time. Physical examination at this time showed an enlarged abdomen, with note of a pelvo-abdominal mass measuring approximately 28 cm × 18 cm, slightly movable, tender on palpation. Pregnancy test was negative. Ultrasound findings showed a large lobulated pelvo-abdominal solid mass measuring 19 cm × 18 cm with minimal ascites. CA 125 was elevated at 241 U/ml. She then underwent emergency exploratory laparotomy, peritoneal fluid cytology, left salpingo-oophorectomy, and complete surgical staging for ovarian new growth probably malignant. Intraoperatively, a massive hemoperitoneum was noted. The left ovary was cystically enlarged to 29 cm × 19 cm × 16 cm, with a thin smooth, white, glistening capsule with noted point of rupture on the anterior ovarian mass measuring 1 cm. The mass contains a necrotic tissue-like substance. The uterus, right fallopian tube, and ovary were grossly normal. Liver and peritoneal surfaces were smooth. Histopathologic examination of the left ovary showed dysgerminoma [Figure 1], with peritoneal fluid and other tissues being negative for malignant cells. The final diagnosis is dysgerminoma, left ovary stage IC2, for which no adjuvant treatment was instituted.

She was followed up every 3 months. An ultrasound surveillance 7 months after revealed a polycystic right ovary with dermoid focus. A repeat ultrasound after 3 months showed a right adnexal mass, to consider ovarian new growth with malignant sonological features. The right ovary measures 3.90 cm × 3.53 cm × 2.14 cm with a solid area measuring 2.55 cm × 2.2 cm × 1.95 cm. Adherent to the right ovary is a solid mass measuring 5.89 cm × 6.76 cm × 4.40 cm with cystic spaces within. Color flow mapping revealed intermediate vascularity [Figure 2].

An exploratory laparotomy was then performed. Intraoperatively, the uterus was small. Minimal adhesions were noted with the omentum and the bowels. The left ovary was surgically absent. The right ovary is converted to a lobulated, pale-tan solid mass measuring 8.5 cm × 8 × cm 6 cm. Peritoneal fluid for cytology was collected. There were no palpable lymph nodes. The surfaces of the liver, subdiaphragm, intestines, and peritoneum were smooth. The appendix was congested. A solid lobulated ovarian mass was resected leaving behind a normal ovarian tissue. The resected mass measured 7.5 cm × 6 × cm 5 cm, which on cut section showed areas of cystic degeneration, hemorrhage, and necrosis [Figure 3]. A rush frozen section revealed dysgerminoma with negative tumor at the resection margins. Lymph node dissection, omentectomy, and appendectomy were subsequently performed. Histopathologic result of the resected right ovarian mass was consistent with dysgerminoma with

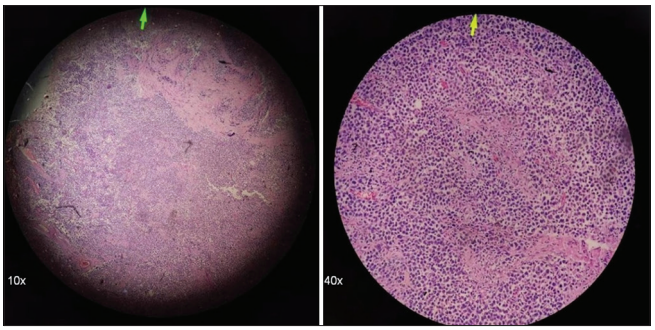


**Figure 1:** Left Ovary. Microscopic view of the left ovary showing Dysgerminoma. Cells are viewed as having clear cytoplasm and central nuclei, with fibrous septations containing lymphocytes seen across the mass

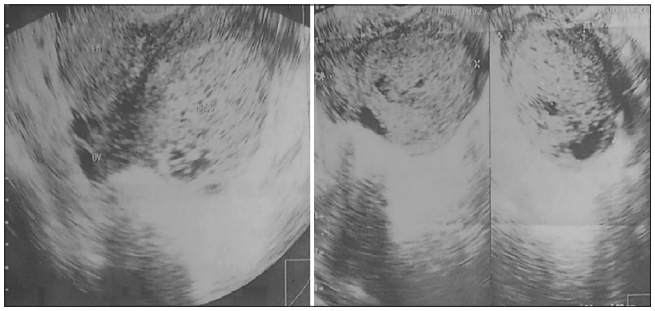

**Figure 2:** Ultrasound of the Right Ovary. The right ovary measures 3.90 x 3.53 x 2.14 cm with a solid area measuring 2.55 x 2.2 x 1.95 cm. Adherent to the right ovary is a solid mass measuring 5.89 x 6.76x 4.40 cm with cystic spaces within

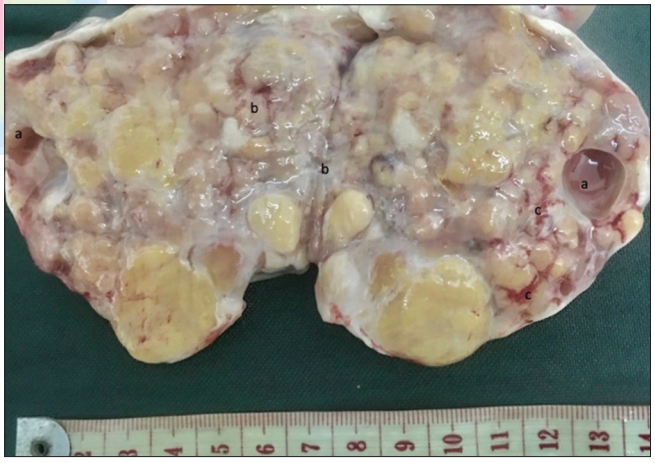


**Figure 3:** Right Ovarian mass. The resected solid mass is lobulated, tan- yellow, measuring 7.5 x 6 x 5 cm. Cut section showed areas of (a)cystic degeneration, (b) necrosis and (c) hemorrhage

noted lymphovascular invasion [Figure 4]. The rest of the tissues submitted were negative for malignant cells.

Three cycles of adjuvant chemotherapy utilizing bleomycin–etoposide–cisplatin (BEP) regimen were administered. After completion of three cycles of chemotherapy, computed tomography (CT) scan was done for surveillance revealing no evidence of tumor residual nor recurrence.

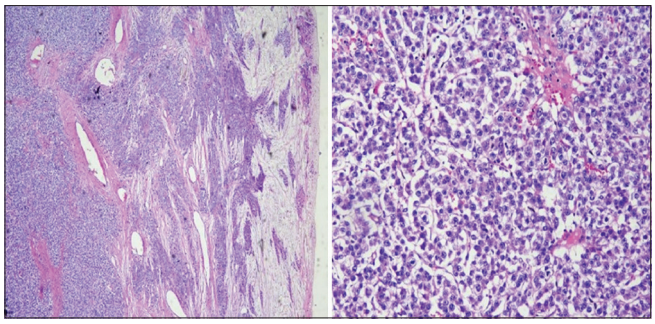

**Figure 4:** Right Ovary. Microscopic view of the right ovary showing Dysgerminoma in low power (left) and high power (right) fields. Still seen are the classic "fried egg" appearance of cells, where the cytoplasm is clear and glycogen-rich, with the nucleus located centrally. Notable are the fibrous septations traversing the mass, with lymphocytes.

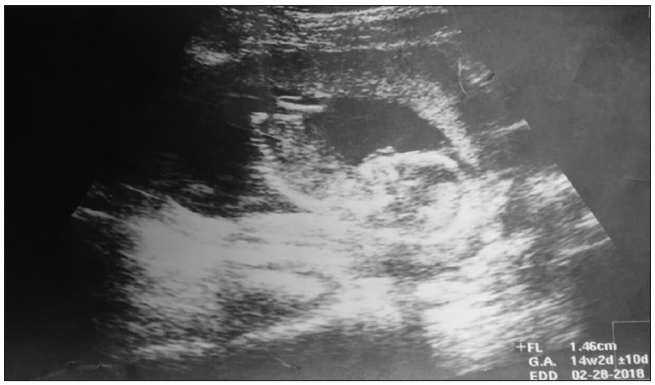


**Figure 5:** Pelvic Ultrasound. Ultrasound showing a single live intrauterine fetus, 14 weeks and 2 days age of gestation by fetal biometry, with good cardiac pulsations

Four months after her last chemotherapy, her beta-human chorionic gonadotropin (HCG) was elevated at 49,700 mIU/ml. A pelvic ultrasound showed a single live intrauterine fetus, 14-week and 2-day age of gestation with good cardiac activity [Figure 5]. Her prenatal consults and fetal surveillance were unremarkable.

Her pregnancy was carried to term with no complications, and she delivered by normal spontaneous delivery to a live term female with a birth weight of 2.85 kg, Apgar score of 8, 9, and Ballard score of 39–40 weeks. At present, the patient has been on continuous follow-up with her gynecologic oncologist, with all her present laboratories and imaging unremarkable. She has had no evidence of disease for 4 years now.

## Case Discussion

Our patient initially had a Stage IC2 dysgerminoma, left ovary which recurred on the contralateral ovary 10 months after the initial surgical intervention. It is said that the simultaneous involvement of the contralateral ovary is low (10%–20%).[3]

Since MOGCT is mostly seen in young patients, as seen in our case, who was diagnosed at 19 years of age, it is recommended that they undergo a surgery which would aim to preserve fertility. Aside from age, patients with nonepithelial ovarian tumors such as MOGCT and sex cord tumors that would undergo fertility-sparing treatment should have the desire to conceive, knowing the risks of the said treatment.[3] These patients should be counseled and be preempted that compliance to follow-up is a must, since close monitoring is warranted. USO, which our patient underwent during her first surgery, is the recommended fertility-sparing surgical treatment,[1,2] especially for early stages of MOGCT. There are several studies which reported that even for advanced stages of MOGCT, fertility-sparing surgery is an acceptable treatment, especially for young women still desirous of pregnancy, since the overall survival rate is high and the recurrence rate is low;[3,4] however, adjuvant chemotherapy must be instituted for these cases.[3] Updated local guideline emphasizes the importance of age and the desire of the patient to get pregnant in managing MOGCT based on their stage. For young patients, and those desirous of pregnancy, USO with complete surgical staging, with or without tumor debulking, is the primary treatment of choice.[2] Adjuvant chemotherapy is instituted for all Stage IA (G1) tumors other than pure dysgerminoma and low-grade (Grade I) immature teratoma.[2] For Stages IA (G2, G3), II–III, and IV, chemotherapy as adjuvant therapy is instituted. External beam radiation therapy is an option for Stage IA (G2, G3), II–III dysgerminoma.[2] For this case, our patient did not undergo any chemotherapy after the first surgery even after note of spillage intraoperatively since the histopathologic samples of the peritoneal fluid and other tissues were negative for malignant cells.

Dysgerminoma responds well to radiotherapy; however, it is now rarely used since it causes premature ovarian failure and decreases the chance of fertility,[3] but there were a few patients with Stage IA dysgerminoma in a study who underwent unilateral oophorectomy and hemipelvic external irradiation who had successful pregnancies after treatment.[5]

Notably, in the first surgery, the contralateral ovary of the index patient was grossly normal. This poses a controversial question on whether a biopsy should have been done to the contralateral normal ovary. Brewer *et al*. have argued that doing an unnecessary biopsy or wedge resection to the normal-looking ovary might result in future infertility and doing a random biopsy to identify microscopic dysgerminoma is especially problematic, even if frozen section examination is to be done.[5] Local guideline also does not recommend doing wedge biopsy in a grossly normal ovary.[2] For the second surgery, the patient underwent wedge resection of the ovarian mass with the frozen section done intraoperatively, which aimed to remove the entire mass and, at the same time,

conserve as much ovarian tissue as possible for future fertility. Wedge resection, in theory, may cause ovarian and peritoneal adhesions which may lead to ovarian failure and future infertility;[3] however, for our case, her fertility was preserved and was able to conceive naturally.

She then underwent adjuvant chemotherapy for a recurrent dysgerminoma with lymphovascular invasion. Chemotherapeutic drugs were already established to cause some damage to the ovary by different mechanisms. Some of which include induction of apoptosis of the primordial follicle pool, ovarian cortex destruction, ovarian atresia, and reduced blood flow to the ovaries.[6] Irreversible ovarian failure which eventually leads to permanent sterility and early menopause is the worst outcome expected after chemotherapy, which may occur several years after completion of chemotherapy.[6] Despite this theoretical knowledge about effects of chemotherapy on ovarian reserve, there are studies which showed ovarian function preservation even with the use of chemotherapy in ovarian malignancies. Successful pregnancy and return of menstrual function were used as measures that ovarian function was preserved. Gershenson *et al*. have collated four studies wherein normal menstrual functions were recorded in at least 80% of patients with MOGCT who underwent fertility-sparing surgery with adjuvant platinum-based chemotherapy, with note of some patients having successful pregnancies.[7] In another study, the pregnancy rate was 75%, and the live birth rate was 65% in those patients who underwent surgery and chemotherapy.[4] Our patient is one of those who had a successful spontaneous pregnancy after two surgeries and chemotherapy.

Premature ovarian failure can be prevented during chemotherapy. The use of oral contraceptive pills (OCPs) and gonadotropin-releasing hormone (GnRH) agonists were noted to have protective effect against chemotherapy-associated premature ovarian failure.[8] Chemotherapeutic drugs, in general, target follicles which result in decreased estradiol levels, increasing the concentration of follicle-stimulating hormone (FSH), which causes accelerated recruitment of follicles which would be continuously destroyed while ongoing chemotherapy, decreasing total ovarian reserve.[8] Administration of GnRH agonist or OCP during chemotherapy may decrease FSH levels which may prevent accelerated atresia of ovarian follicles[8] [Figure 6]. Suppression of the hypothalamic–pituitary axis by GnRH agonist may simulate the prepubertal state of quiescent gonads making the ovary less susceptible to the cytotoxic effects of chemotherapy.[9] Botha published a review regarding the use of OCP during chemotherapy in three studies, which showed that OCP does not protect the ovary from the gonadotoxic effects of chemotherapy, especially with older women and the use of high-dose alkylating chemotherapeutic agents.[10] Patients in these studies developed chemotherapy-induced menopause, amenorrhea, and oligomenorrhea; however, the involved studies had small sample size.[10] A larger study was mentioned in the review wherein not taking OCP during chemotherapy was found to be one predictor of amenorrhea.[10] This review also included studies which compared incidences of ovarian failure with and without the use of GnRH agonists. Twelve studies showed that the incidence of ovarian failure with the use of GnRH agonists was lower as compared to the control group.[10] Our patient did not receive any hormonal treatment for prevention of premature ovarian failure.

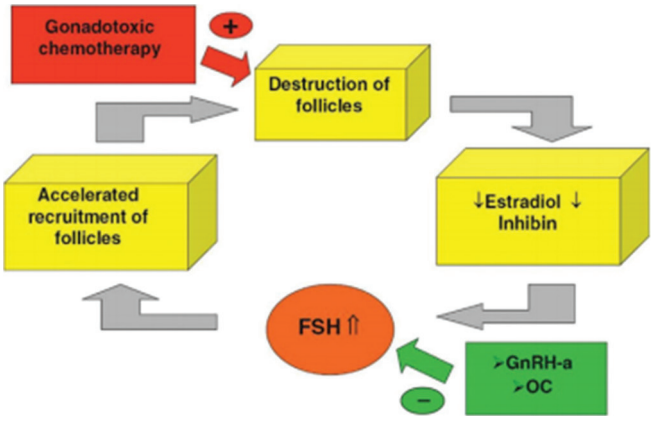


**Figure 6:** Mechanisms on how GnRH agonist and Oral Contraceptives may possibly prevent premature ovarian failure. These two agents would potentially decrease FSH levels preventing accelerated atresia of follicles preventing premature ovarian failure[8]

With the advent of modern technology, there are now several options for fertility preservation using assisted reproductive technology (ART) before initiation of treatment.[6] The use of ART requires detailed assessment and counseling of the patient as to her available options, combined with realistic discussions regarding success rates of these treatments.[6] Embryo, oocyte, and ovarian tissue cryopreservation are some of the options for preservation.[6]

Even after treatment, apprehensions of couples planning for pregnancy may arise on the concerns regarding potential teratogenic effects of chemotherapy. Oocytes, during their rapid development before ovulation, are most vulnerable to chemotherapeutic agents, and might potentially cause mutation and oxidative damage leading to teratogenicity; however, no such outcomes in humans were noted as in the study presented.[6] Hyman *et al*. reported that following chemotherapy, they advise patients to wait for 6–12 months before conception.[6] Our index case had her conception 4 months after the last cycle of chemotherapy, and there were no apparent

abnormalities in the development of her child who is 2 years old now.

In terms of surveillance after treatment, the Society of Gynecologic Oncologists of the Philippines suggested that follow-up must be done every 3 months for the first 2 years, then every 4–6 months in the 3rd year, every 6 months for the next 2 years, and then yearly thereafter. For every visit, physical examination, including bimanual pelvic and rectovaginal examination, must be done. Especially for patients who underwent fertility-sparing surgery, pelvic ultrasound scans every 6 months should be done, with appropriate tumor markers every visit, such as serum β-HCG and alpha-fetoprotein. Additional diagnostics must be done once with elevated tumor markers, such as holo-abdominal with transvaginal ultrasound with or without color Doppler studies, chest X-ray if with signs or symptoms, CT scan, magnetic resonance imaging, positron emission tomography-CT scan, bone scintigraphy, and chest CT scan as indicated.[2] These posttreatment surveillances are necessary for early detection of relapse so that timely and appropriate planning of treatment be delivered. Good compliance and follow-up of our patient contributed greatly to the success of managing her case since recurrence of the dysgerminoma on the remaining ovary was immediately detected and managed accordingly.

Having this disease has a lot of psychological impact on these patients, which is why it is also important to address these issues with every visit of these patients. As physicians, our ability to give support to our patients might just lead to a better quality of life.

## Summary

The case narrates how a patient initially had a unilateral dysgerminoma which recurred on the contralateral ovary after USO who eventually underwent a fertility-sparing surgical removal of the mass and underwent the BEP regimen chemotherapy. With dysgerminoma being the most common MOGCT among adolescents and young adults, preservation of fertility is the goal. Despite two consecutive surgeries, with adjuvant chemotherapy, our patient had a successful pregnancy, which could give us a good insight on how to manage future cases similar to our patient, with emphasis on preservation of one's fertility. It is important to counsel patients about their condition, the treatment options they have, and the possible outcomes of these interventions. Being able to give the best care, we could offer these patients as physicians would bring about a better quality of life for these patients.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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