



# Non-gestational Ovarian Choriocarcinoma in a Virgin Woman: A Case-Report

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## Abstract

A 21-year-old Iranian female presented to hospital with irregular menstruation, heavy menstrual bleeding and severe secondary dysmenorrhea for three years with a history of primary amenorrhea was referred to gynecology oncology section. Suspected cystic lesion with homogenous internal echo measuring about 31\*24 mm in the right adnexa was diagnosed with ultrasound examination and  $\beta$ -HCG was reported 2000 IU. Patient was treated with right oophorectomy in February of 2019. The patient was referred to a gynecologist due to relapse in march of 2019 (1 months after oophorectomy). This time gynecologist, after consulting with an oncologist, began chemotherapy instead of surgery for this patient. Four courses chemotherapy treatment with Etoposide 100 mg/500N/S/ 2hours, Cisplatin 35 mg/500 cc N/S/ 2 hours and Bleomycin 15mg/500 N/S/2hours was prescribed for this case of ovarian choriocarcinoma since March of 2019. After chemotherapy  $\beta$ -HCG was reported 2IU. After 6 months of chemotherapy, sonography was normal and there was no recurrence sign in CT-scan.

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## Introduction

Ovarian Germ Cell Tumors (OGCTs) are derived from primordial germ cells of the ovary. OGCTs are divided in two groups of benign and malignant. These neoplasms comprise approximately 20 to 25 percent of ovarian neoplasms overall, but account for only about 5 percent of all malignant ovarian neoplasms [1]. OGCTs arise primarily in young women between 10 and 30 years of age and represent 70 percent of ovarian neoplasms in this age group [2].

OGCTs can be divided into those that differentiate toward embryo-like neoplasms (teratomas and their subtypes and dysgerminomas) and those that differentiate primarily toward extraembryonic fetal-derived (placenta-like) cell populations. OGCTs can also be a mixture of both [1].

Choriocarcinoma can arise in one of three ways: as a primary choriocarcinoma associated with ovarian pregnancy; as a metastatic choriocarcinoma from a primary gestational choriocarcinoma arising in other parts of the genital tract, mainly the uterus; and as a germ cell tumor differentiating in the direction of trophoblastic structures and mixed with other neoplastic germ cell elements. A tumor arising in the latter is classified as a non-gestational choriocarcinoma [3].

Among malignant OGCTs, dysgerminoma, immature teratoma, yolk sac tumors, and mixed germ cell tumors account for 90 percent of cases [4]. Pure embryonal carcinomas and Nongestational Choriocarcinomas (NGCO) are rare, and pure polyembryomas are very rare [5].



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Nongestational choriocarcinoma is a rare and highly malignant type of OGCT [6]. Choriocarcinomas are more commonly originated from placenta; the estimated incidence of a primary ovarian choriocarcinoma is 1 in 369,000,000. They comprise 2.1 percent of all malignant OGCTs [7]. A choriocarcinoma of ovarian origin derives from an extraembryonic differentiation of malignant germ cells. This highly malignant germ cell epithelial neoplasm differentiates towards trophoblastic structures and often contains other malignant germ cell elements. Nongestational ovarian choriocarcinoma is histologically identical to primary gestational choriocarcinoma associated with pregnancy [3].

Nongestational choriocarcinoma arises in women under 40 years old, and the frequency is reported less than 0.6% of all ovarian tumors [5].

It is difficult to diagnose ovarian choriocarcinoma as gestational or non-gestational except in patients who are sexually intercourse. DNA analysis is a reliable method for distinguishing gestational tumors from nongestational tumors. It is reported that the genetic origin could be determined by using only two or three appropriate variable numbers [8].

The measurement of Beta-Human Chorionic Gonadotropin (B-HCG) would help in the preoperative diagnosis and estimation of serum  $\beta$ -hCG levels is suggested in the diagnostic work-up of young female and female in reproductive age group [8].

Gestational Choriocarcinoma (GCO) is treated with methotrexate-based chemotherapy such as: MEA (Methotrexate, Etoposide and Actinomycin-D), EMA/CO (methotrexate, etoposide, actinomycin-D, cyclophosphamide and vincristine), or EMA/EP (etoposide, cisplatin, methotrexate and actinomycin-D). However, nongestational ovarian choriocarcinoma (germ cell tumor) is so rare that there is lack information on therapeutic options. In young patients, stage I germ cell tumors can be treated with conservative surgery, i.e., unilateral oophorectomy or salpingo-oophorectomy. Postoperative chemotherapy is recommended by combination chemotherapy with the BEP (bleomycin, etoposide and cisplatin) or methotrexate-based regimen [9].

Through this paper, the authors present a case summary of a 21-years-old woman single virgin with nongestational ovarian choriocarcinoma treated with oophorectomy and postoperative chemotherapy.

This patient was treated with chemotherapy at relapse. Because this disease is a very rare cancer and the patient in relapse phase responds well to the treatment, we decided to introduce the case in the form of this report.

### Case Presentation

A 21-year-old female with irregular menstruation, heavy menstrual bleeding and severe secondary dysmenorrhea for 3 years with a history of primary amenorrhea was referred to gynecology oncology section. her period began when she was 17 years old, after drug treatment. The patient was virgin and without any kind of sexual contact according to her history.

The report of an ultrasound examination for 5 months ago (September of 2019) was observed in the medical records of patient, in which it was stated that Suspected cystic lesion with homogenous internal echo measuring about 31\*24 mm in the right adnexa.

In February of 2019 the patient presented with acute abdominal symptoms and  $\beta$ -HCG was reported 2000 IU. Patient was treated with emergency right oophorectomy in February of 2019.

The frozen section of the specimen was not sent to the pathology during the surgery because the patient has referred to a general hospital as an emergency during the afternoon shift and it was not possible to send the frozen section at this time and after the surgery. The removed mass was sent to the pathological laboratory.

The entire right ovary was removed because the surgeon had a strong suspicion of germ cell mass and healthy ovarian tissue was not visible on the right side, at the same time, the left ovary was perfectly healthy, therefore the entire right ovary has been removed.

In microscopy and macroscopy report, the size of the mass that was located in right ovary was estimated 9\*5 cm. A well-defined mass was removed. Consisted of extensive necrosis and hemorrhage with viable tumoral cells composed of scattered multinucleated syncytiotrophoblastic cells admixed by cytotrophoblastic cells (Figure 1).

The patient was referred to a gynecologist due to relapse in march of 2019 (1 months after oophorectomy). In the CT-scan report, various hypodense lesions are observed with peripheral enhancement, tubular and nodular pattern in the adnexa in favor of neoplastic changes. This time gynecologist, after consulting with an oncologist, began chemotherapy instead of surgery for this patient (Figure 2).

The Treatment includes four courses chemotherapy with Etoposide 100 mg/500N/S/ 2 hours, Cisplatin 35 mg/500 cc N/S/ 2 hours and Bleomycin 15mg/500 N/S/ 2 hours was prescribed for this case of ovarian choriocarcinoma since March of 2019.

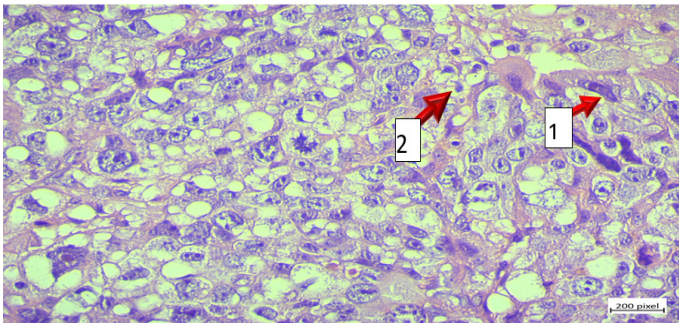
Also GnRH agonist (Zoladex) was prescribed to protect the other ovary from the side effects of chemotherapy and to maintain the patient's fertility during chemotherapy.

It should be noted that germ cell tumors are very invasive tumors and chemotherapy surgery should be started immediately, even before the wound has healed. However, in this case, the pathology result was prepared late and also the patient did not agree to the chemotherapy, so the mass was sent again to another pathologist and there was a delay in starting chemotherapy until the second pathology result was prepared.

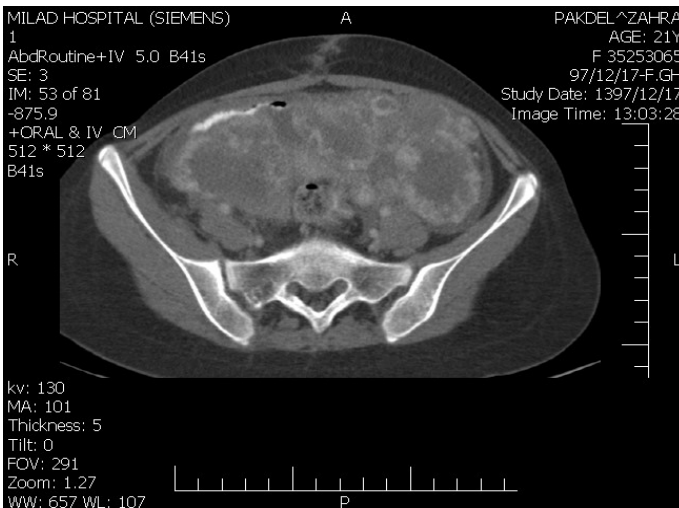
The patient did not experienced any serious complication during chemotherapy. She had experienced anemia (Hb=10.7) and thrombocytopenia (570 10e3/ $\mu$ l) only in one period, which was resolved by Pegagen administration.

After chemotherapy  $\beta$ -HCG was reported 2IU.

After 6 months of chemotherapy, sonography was normal and there was no recurrence sign in CT-scan (Figure 3).



**Figure 1:** Choriocarcinoma.  
1. Syncytiotrophoblast.  
2. Cytotrophoblast.



**Figure 2:** Adnexa in CT-scan after surgery and before chemotherapy.



**Figure 3:** Adnexa in CT-scan after chemotherapy.

**Discussion**

Ovarian choriocarcinoma -an exceeding rare germ cell tumor-is considered to be aggressive in nature and most patients with this tumor are usually young [10].The distinction between NGCO and GCO is warranted because of the worse prognosis of NGCO. NGCO requires more aggressive therapy with multiple chemotherapeutic agents [11].

Choriocarcinoma is characterizes biochemically by the production of the Human Chorionic Gonadotrophin (HCG) in the absence of an ongoing pregnancy [12]. As  $\beta$ -hCG of this patient was calculated to be 2000 IU. although in our case report  $\beta$ -Hcg increased, but in other case reports  $\beta$ -Hcg was further increased. As can be seen in the case report by Balat et al,  $\beta$ -hCG was 1,787,052. Also in Lin's study  $\beta$ -Hcg was 279,000 [13].

As these tumors are rare, treatment recommendations for primary extraovarian, nongestational choriocarcinoma are not available. In young patients, stage I germ cell tumors can be treated with conservative surgery, i.e., unilateral oophorectomy or salpingo-oophorectomy. Postoperative chemotherapy is recommended by combination chemotherapy with the BEP (bleomycin, etoposide and cisplatin) or methotrexate-based regimen [9]. In a case that Bazot reported, 21 years old patient received chemotherapy but she dead after 1 curse of chemotherapy [14]. However Gon,Hayashi,Rao the patients treated their patients with BEP regimen [15].

We initiated the treatment with multi agent chemotherapy after relapse, and the response after 4 courses chemotherapy was perfect. The serum  $\beta$ -hCG level fell to within the normal range and the latest  $\beta$ -hCG has reported 2 IU. Although some patients die because of the complication of chemotherapy like sepsis [13] but our patient did not complain of any problem after 6 months.

As a limitation of this patient's management, it should be noted that we could not send a frozen section during the afternoon shift when the patients was admitted to the hospital; it is also best for patients with menstrual problems and large tumors to see a doctor sooner before they need emergency surgery. And it is better to start chemotherapy very soon after surgery.

**Conclusion**

Non-gestational choriocarcinoma in ovary is a rare tumor. Serum  $\beta$ -hCG, CT scan and pathology specimen with sytotrophoblastic cells are helpful in diagnosis.

At the time of recurrence, the patient usually responds to chemotherapy and does not require surgery, if the decision is made with multidisciplinary treatment and we can maintain the patient's fertility.

The presence of gynecological oncologist and hemato-oncologist also helps to treat patients with only chemotherapy and without the need for repeated surgery. It is necessary to have surgery for the first time but because of well response to chemotherapy, managing these patients at the recurrence time by team and carefulness to maintain efficiency is required.

**Declaration of Patient Consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient is aware that her name will not be published.

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