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Dysgerminoma with Pregnancy: A Rare Ovarian Tumor Case Report

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Abstract: ***A case, 24 year old Balinese womanpregnant woman G3P1011 was from Sanglah General Hospital, Bali, Indonesia. She was gravida 29 week with Dysgerminoma. Measurements were made on CA 125, AFP, USG abdomen. Frozen section, left Salfingo-oopharectomy and omentectomy were done preserving the pregnancy. The result of histopathology examination of paraffin block on tuba and ovarium sinistra, omentum and cytology of ascites fluid after surgical removal was ovarian dysgerminoma stage IC. The immunochemistry staining CD 117 confirmed the diagnosis of ovarian dysgerminima.***

Keywords: Dysgerminoma of ovary, Pregnancy

1. Introduction

Pregnancy with dysgerminoma type ovarian cancer is a very rare condition, as evidenced by the lack of scientific publications that discuss the case.Disgerminoma is the most common ovarian cancer found in pregnancy, where 2-3% of the mass in the ovaries detected during pregnancy is cancer ovary. Another literatures mention the incidence of ovarian cancer in pregnancy was 4 untill 8 of 100, 000 pregnancies. The incidence increases by the increasing quality of antenatal examination.[1, 2, 3] Germ cell tumors are around 70% of ovarian tumor cases, occurring during the first decades of life, manifest with malignant characteristics in 1/3 of cases and are rarely found after this period.Dysgerminomas are non epithelial ovarian tumors derived from ovarian germ cells. Dysgerminomas are very rare but are the most common germ cell tumors of any type, often found in the early stages and in young age, and are responsible for about 10% of ovarian cancer cases.[4, 5, 6]

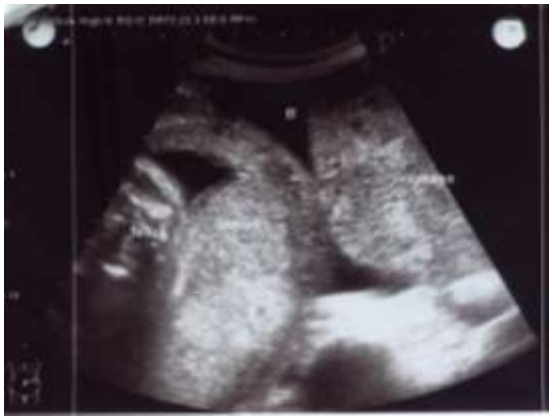
Most dysgerminomas are unilateral and occur predominantly on the right side, but around 12 percent of cases may be bilateral. Dysgerminoma is the most common malignant germ cell tumor, accounting for 30-40% of all ovarian cancers derived from germ cells. They represent only 1-3% of all ovarian cancers, but represent as many as 5-10% of ovarian cancers in patients under the age of 20. About 65% of Disgerminomas are diagnosed in stage I and 85-90% of these tumors are limited to one ovaries, while 10-15% are bilateral. Other germ cell tumors are rarely bilateral. In patients whose contralateral ovaries are conserved, dysgerminoma may occur around 5-10% over the next 2 years.[7]

The diagnosis of pregnancy with dysgerminoma confirmed by histopathology, ultrasound examination and the serum tumor marker is the one of the diagnostic criteria for predicting disgerminoma type ofovarian cancer. Ultrasonography has a 90% sensitivity, 90% specificity, 69% predictive value (PPV) and 97% negative predictive value (NPV) in determining the ovarian mass suspected of a malignant suspicious ovarian cyst.[8, 9] Ultrasound imaging combination with CA125 increases the sensitivity untill 93, 7 to 95.6% and the specificity 91.1 to 100%. [10]

2. Case Report

A 24 year old G3P1011 was from Sanglah General Hospital, Bali, Indonesia. She was gravida 29 week. Based on clinical data, laboratory tests, ultrasound examination, frozen section and histopathology examination this case was diagnosed as dysgerminoma in pregnancy. Dysgerminoma is a rare condition, with poorly understood behavior during pregnancy. The incidence of ovarian cancer during pregnancy is 4:100, 000. The incidence increases along with the quality of antenatal examination. Pregnancy coincided with dysgerminoma cause impact to pregnancy itself, on the fetus, and dysgerminoma progression.

Ultrasound examination showed a solid mass at left adnexa with diameter 11.17cm. Tumor marker tests on Alpha- Fetoprotein(AFP) 135, 48 (N < 8, 0 IU/mL), Cancer Antigen 125 (CA 125) 113, 44 (N < 35 U/mL), Human Epididymis Protein 4 (HE4) 68, 9, Risk of Malignancy Index (RMI) 340, 32, yhe Risk of Ovarian Malignancy Algorithm (ROMA) 99, 37%.



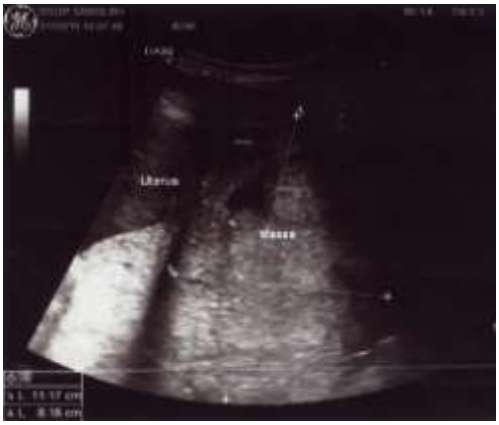


Figure 1: Ultrasonography revealed a pregnancy and Ovariunsolid tumor

The patient had normal delivery. Surgical staging performed on post-partum day 42. Patient undergone frozen section, total abdominal hysterectomy-salphyngoovarectomy dextra (TAH-SOD) and performed histopathology examination. Evaluation of nodules in omentum was negative, performed omentectomy and evaluation of lymph nodes and no enlargement occurs. Histopathology examination and immunohistochemistry staining were positive, that was consistent with dysgerminoma. The cytology examination from ascites fluid was positive malignant cells.

Pathological Findings

Macroscopic examination: An ovarian mass of 19 cm x 16 cm x13cm in size, bosselated outer surface and intact capsule. Cut section showed a solid and cyst, white and tan colored mass along with foci of hemorrhage and necrosis (Figure 1).The tumor was infiltrative to the ovarian capsule.

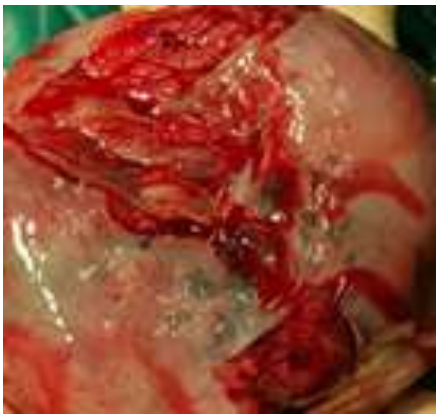


Figure 2: Grossly cut section showed solid mixed with cystic mass of left ovarian, tan colored growth with foci of hemorrhage and necrosis

Microscopic examination: Tissue sections of the mass showed well defined nests of polygonal to round cells, uniformly size with clear cytoplasm, medium size vesicular nuclei and prominent nucleoli, some mitosis, separated by thin fibrous septa that contain lymphocyte inflammatory cells. The fallopian tube was normal. The malignant cells were present in the peritoneal fluid. Immunochemistry staining showed CD 117 positive in membrane cell for Dysgerminoma.

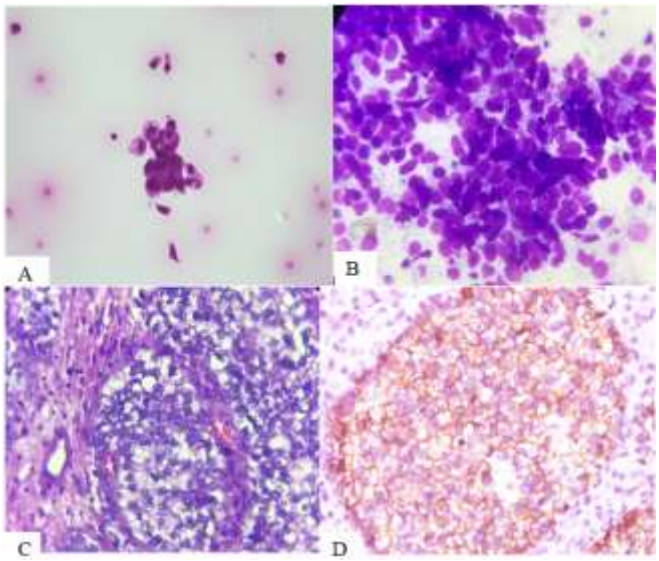


Figure 3: Cytologic examination of ascites fluid showed malignantcells, papanicuolou (400x) (A). Inprint: Scattered of malignant cells. Diff kwik(400x)(B).Histopathologic examination showed polygonal to round cells, uniformly sizewith clear cytoplasm, medium size vesicular nuclei and prominent nucleoli, some mitosis, separated by fibrous strands containing lymphocyte inflammatory cells HE (400x) (C). Immunohistochemistry staining CD 117 was positive in membrane cells (400x) (D).

Histopathologically, dysgerminomas usually consist of sheets or 'nests' of polygonal cells with eosinophilic cytoplasm to clear and different cell membranes. The tumor cells have a uniformly large uniform core with vesicular chromatin, located in the middle and prominent nucleoli.Membrane typical nucleus ("squared off") .Total number of mitoses.Tumors are usually separated by thin connective tissue containing infiltration of lymphocyte inflammatory cells (mostly T cells) and epithelial histiocytes that can form sarcoid-like granulomas.Lymphocytes and hisitocytes epitheloid (rare) spread among tumor cells. About 3% of dysgerminomas contain giant syncytiotrophoblast cells that are directly derived from dysgerminoma cells without any cyto-trophoblast involvement. Some tumors exhibit a broad necrotic focus that may indicate dystrophic calcification. In this case the histopathologic examination results revealedthe morphology apropriate for dysgerminoma.

Further planning to this patient was continuing the *mode of delivery* as obstetrical indication. Plan also to do a sectio caecarian if needed and relaparatomy surgical staging (simultaneously) at 38 weeks of gestation. Chemotheraphy will performe and still waiting the pregnancy reaches 38 weeks of gestation. Oncogynaecology division performed the chemotherapy by giving 4 series as the protocol.

The Patient inpartu by normal (pervaginam) delivery, healthy male baby was born with body weight 2100 gram. Surgical staging performed on post partum day 42. After delivery, performed surgical staging for relaparatomy:

Large uterine identification and normal consistency. Performed total abdominal hysterectomy-salfingoooforectomy dextra (TAH-SOD) and performed histopathology examination. Evaluation of nodules in omentum (-), performed omentectomy, evaluation of lymph nodes and no enlargement occurs.

3. Discussion

To establish the diagnosis ofpregnancy with ovarian cancer IC type of dysgerminoma is quite difficult, because the diagnosis of dysgerminoma is made by histopathologic examination in which this involves an invasive procedure, through laparotomy surgical staging.[10]Although some journals suggest that surgical removal procedures adnexa during pregnancy is safe for mothers and infant outcomes, but other journals mention the rate of spontaneous abortion in first trimester and premature delivery in the third trimester increases.[11, 12]The diagnosis of ovarian cancer IC type dysgerminoma in this patient is enforced after histopathologic examination after conservative laparatomy surgery and omentectomy as well as cytology of ascites fluid at 29 weeks 6 days.

The lack of reports on pregnancy cases with ovarian cancer results in at least some data on the effect of pregnancy on ovarian cancer. Based on existing case reports, although pregnancy does not affect the prognosis of an ovarian tumor, torsion of ovarian tumors may occur. Types of adnexal mass during pregnancy of 10-15% occur most often at week 8 to week 16 when the uterus enlarges rapidly. The incidence of ovarian torsion in the third trimester of pregnancy is 5.9%. Ovarian torsion may cause acute abdominal and fetal loss especially during first trimester pregnancy.[11-13]

Ovarian dysgerminomas need to be diagnosed accurately because its treatment and prognosis differs considerably from other ovarian neoplasms. Dysgerminomas has a better prognosis and greater sensitivity to available treatment modalities among all ovarian neoplasms. Cure rate approaches almost 95% employing conventional treatment options.Dysgerminoma is one of the two most common malignant germ cell tumors of the ovary.Still, it accounts for only 1-2% of all malignant ovarian tumors. Dysgerminoma occurs mainly in children and young women. The average age is 22 years, and 90 percent of patients are less than 30 years of age. About 20 percent of malignant ovarian tumors detected during pregnancy are dysgerminomas. The usual presentation is with nonspecific findings such as abdominal distention, an abdominal mass, or abdominal pain. Some patients have menstrual abnormalities or gastrointestinal or urinary symptoms. Rare patients have hypercalcemia. Serum lactic dehydrogenase (LDH) is frequently elevated but increased levels of serum alpha- fetoprotein or human chorionic gonadotropin are generally not detected. If increased, they suggest that other germ cell elements are present in the tumor. Of note, however, about 3% of patients with a pure dysgerminoma have increased amounts of beta-hCG in the blood, secreted by syncytiotrophoblastic cells within the tumor. Dysgerminoma is the most common malignant gonadal tumor in patients with gonadal dysgenesis. Dysgerminoma is confined to the ovaries (stage I) at diagnosis in 60–80 percent of patients. It is usually unilateral, which is characteristic of all malignant germ cell tumors.

Dysgerminoma is unique among these tumors in that it is the only one with a significant incidence of bilaterality; both ovaries contain tumor (stage IB) in 5–15 percent of cases. The tumor in the contralateral ovary is grossly visible in half of the bilateral cases and it is a strictly microscopic finding in the other half. Some oncologists recommend biopsy of an apparently normal contralateral ovary if treatment is to be by unilateral salpingo-oophorectomy only. Dysgerminoma metastasizes via the lymphatics to the paraaortic lymph nodes, with subsequent spread to the mediastinal lymph nodes, and by transperitoneal spread to the pelvic and abdominal peritoneum. [13, 14]

Unilateral encapsulated dysgerminoma (FIGO stage IA) can be treated by salpingooophorectomy with a 5-year survival rate of greater than 90 percent. Postoperative therapy has been advocated for patients with localized disease, but there is an increasing trend to follow such patients closely and administer chemotherapy only to those who develop a recurrence. Recurrences can usually be successfully managed. When dysgerminoma develops in a dysgenetic gonad, the appropriate treatment is bilateral gonadectomy. The standard treatment for advanced disease (stage >IA) is total abdominal hysterectomy, bilateral salpingo-oophorectomy, limited debulking, and postoperative chemotherapy or radiotherapy. If they are not involved by tumor, the uterus and the contralateral ovary may be conserved in young patients when preservation of fertility is important. Chemotherapy with platinum-based regimens is highly effective against dysgerminoma and is less likely than radiation to cause ovarian failure and infertility. Overall survival of optimally treated patients now exceeds 90 percent. Recurrences usually become evident within two years of primary treatment. [14, 15]

Table 1: FIGO classification of ovarian tumor [11]

Stage I. Tumor confined to ovaries or fallopian tube(s)
T1-N0-M0
IA: tumor limited to one ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
T1a-N0-M0
IB: tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings
T1b-N0-M0
IC: tumor limited to one or both ovaries or fallopian tubes, with any of the following:
IC1: surgical spill
T1c1-N0-M0
IC2: capsule ruptured before surgery or tumor on ovarian or fallopian tube surface
T1c2-N0-M0
IC3: malignant cells in the ascites or peritoneal washings
T1c3-N0-M0
Stage II. Tumor involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer
T2-N0-M0
IIA: extension and/or implants on uterus and/or fallopian tubes and/or ovaries
T2a-N0-M0
IIB: extension to other pelvic intraperitoneal tissues
T2b-N0-M0
Stage III. Tumor involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes
T1/T2-N1-M0
IIIA1: positive retroperitoneal lymph nodes only (cytologically or histologically proven):
IIIA1(i) Metastasis up to 10 mm in greatest dimension
IIIA1(ii) Metastasis more than 10 mm in greatest dimension
IIIA2: microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
T3a2-N0/N1-M0
IIIB: macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
T3b-N0/N1-M0
IIIC: macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumor to capsule of liver and spleen without parenchymal involvement of either organ)
T3c-N0/N1-M0
Stage IV. Distant metastasis excluding peritoneal metastases
Stage IVA: pleural effusion with positive cytology
Stage IVB: parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)
Any T, any N, M1

Chromosome 12p abnormalities are present in many malignant germ cell tumors. The most common abnormality is an isochromosome, i12p, but over-representation of chromosome 12p material is sometimes found present in addition to or instead of an i12p. In one study, an i12p was identified in 16 of 21 dysgerminomas and over-representation of chromosome 12 material was detected in 5 dysgerminomas.[14]c-KIT mutations have been identified detected in about 25% of dysgerminomas, but they are located in exon 17, not the exon 11 location that confers sensitivity to imatinib. There is no correlation between the presence or absence of a c-KIT mutation and immunohistochemical staining for CD117. Numerous immunohistochemical stains are available to confirm a diagnosis of dysgerminoma. These falls into two main groups: antibodies against cytoplasmic and membranous antigens and antibodies against nuclear antigens. The first group includes placental alkaline phosphatase (PLAP), CD117 (c-kit) and D2. All are excellent markers for dysgerminoma. The expression of c-kit (CD117) has been demon- strated in a wide variety of human malignancies, including those of the lung, breast, endometrium, gastrointestinal tract, urinary bladder, and hemato- poietic system. Dysgerminoma is a relatively rare malignant germ cell tumor of the ovary seen in young adults. In this study, we demonstrate that 87% of these tumors exhibit immunohistochemical expression of the transmembrane tyrosine kinase receptor c-kit (CD117) much like its male counterpart, seminoma. Thus, immunostains for c-kit may be potentially useful in distinguishing between dysgerminoma and other ovarian neoplasms.[15, 16]In this case, it was positive for CD 117 imunohisthochemistry examination.

4. Management

Based on some studies, the removal of adnexal masses during pregnancy is safe for both the mother and the fetus.[12] Second trimester pregnancy is the 'safe period' or the best time to intervene adnexa mass surgery because at this time the dependence of hormone secretion during pregnancy from corpus luteum is reduced so that the risk of spontaneous abortion is low.[2, 3] The tocolytic agents may be given before or immediately after surgical intervention and continued 24 to 48 hours post-surgery.[2] The surgical removal of adnexal masses performed during pregnancy is a conservative surgery of unilateral oophorectomy or cystectomy for histopathologic diagnosis.In advanced stage (stage II-IV) considered for termination of pregnancy before 24 weeks is followed by adnexal mass removal and chemotherapy .[2, 3, 6]The main challenge in the management of cancer chemotherapy in pregnancy is giving the optimal anti cancer treatment without disturbing the development of the fetus.

5. Conclusion

Pregnancy with ovarian cancer is a rare case. The prognosis depend of the early stage of diagnosis.Based on clinical data, laboratory test, USG, frozen section, histopathology examination and immunochemistry staining, this case was diagnosed as dysgerminoma in pregnancy. Detected at an early stage, the 5 years survival rate can reach 90-95%. Chemotherapy given with very carefully. The success of therapy is determined by early diagnosis at the early stage, prompt histopathologic, the routine antenatal care (ANC) and the using of ultrasound examination.

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