Primary Ovarian Non-Hodgkin's Lymphoma: A Case Report of a 31-Year-Old of Bali Woman

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Abstracts: Background: Primary ovarian Non-Hodgkin's lymphoma is a rare disease that is difficult to diagnose because it is often mistaken for ovarian cancer. Case presentation: A 31-year-old Bali woman presented abdominal pain for 2 days and experienced weight loss. USG image showed a solid mass with multiple internal cystic components on the right adnexa, measuring the mass in the right adnexa 6.8 x 6.1 cm, suggesting a mass of the right ovary and para-aortic multiple lymphadenopathies. The patient underwent a complete blood count test, blood chemistry test, and tumor marker laboratory results showed an increase of cancer antigen 125 and lactate dehydrogenase, with normal value of cancer antigen 19-9, serum of β-human chorionic gonadotropin, and alpha-fetoprotein. Minimal pleura effusion was also found on the left side. The patient diagnosed with a malignant ovarian tumor was planned for a USO-FZ laparotomy. Laparotomy was performed in the internal genitalia, a solid tumor originating from the right ovary, size 10 x 10 cm was found and the left ovary appeared to be 4 x 5 cm. Nine days after laparotomy, the diagnosis showed a diffuse large B cell lymphoma. The patient was transferred to the hematology division and scheduled to undergo chemotherapy. Conclusion: Diagnosis is a crucial step in handling this case. Primary ovarian NHL is a difficult case to diagnose because it can be mistaken for other genital malignancies.

Keywords: primary ovarian lymphoma, ovarian lymphoma, non-Hodgkin’s lymphoma, case report

1. Introduction

Non-Hodgkin's lymphoma (NHL) is a large group of primary malignancies derived from lymph nodes and extra-nodal lymphoid tissue, which can originate from B lymphocytes, T lymphocytes, and natural killer cells.¹ Primary Non-Hodgkin's lymphoma that occurs in gynecological organs is a very rare case, only about 1%. The ovaries are the most common locations in the genital organs that develop lymphoma.² Non-Hodgkin's lymphoma is the seventh most common malignancy and eighth as a cause of cancer death. Data from the Ministry of Health of the Republic of Indonesia shows that NHL together with Hodgkin's lymphoma and leukemia are in the 6th rank of malignancy.¹ Approximately 7% to 26% of cases of ovarian malignancy, especially NHL, show involvement of the ovarian organs.³ ⁴

It is difficult to distinguish between primary or secondary ovarian lymphoma. Primary ovarian Non-Hodgkin's lymphoma (PONHL) is very rare because the ovaries have less lymphatic tissue.⁵ Diffuse Large B-cell lymphomas (DLBCL), are the most common cause of NHL in genital tract lymphoma, which is about 25% of cases.³ Other types of lymphoma found in the ovaries are Burkitt and follicular.³ ⁶ ⁷ Ovarian lymphoma can occur at any age, ranging from 21 to 69 years, but mostly occurs at the age above 40 years.² ³ The most common clinical presentations of ovarian NHL are abdominal pain, vaginal bleeding, and adnexal masses. Only about 10% -33% of patients show classic B cell symptoms, such as fatigue, fever, night sweats, and weight loss.² ³ Several case reports showed a homogeneous, bilateral adnexal mass, absence of ascites and tumor size>5cm at the time of diagnosis as clinical features associated with primary ovarian lymphoma.⁵ ⁸

The prognosis of ovarian lymphoma is often poor due to late diagnosis. PONHL has a poor prognosis with a range of 0% to 36% surviving for 3 years.⁹ In some of the reported cases, the patient underwent radical surgery with a suspected diagnosis of epithelial ovarian malignancy, even though a correct diagnosis could allow optimal treatment, namely chemotherapy, not radical surgery. Therefore, gynecologists should be more aware of the presentation of a rare case like this.³ ¹⁰

2. Case Presentation

A 31-year-old female patient who came on (April 28th 2020) complained of abdominal pain for approximately 2 days. The patient also feels weight loss despite the usual appetite for eating and drinking. Patients with a history of hospitalization at Sanglah General Hospital (19/04/2020 - 23/04/2020) due to bilateral pleural effusions. The radiological image of the mass in the right adnexa measuring 8.6 x 6.1 cm was accidentally found during abdominal ultrasound (21/04/2020). The patient also showed elevated levels of the cancer antigen (CA) 125 to 1449, then the patient diagnosed with a malignant ovarian tumor was planned for a USO-FZ laparotomy. On physical examination of the abdomen, there was also a solid mass measuring 10x10 cm, flat surface, firm boundaries, limited mobility, and no pain. The patient has a fever fluctuating with a temperature of around 37-38.8°C. Fever in the patient was accompanied by laboratory results of thrombocytopenia (65.76) so that the differential diagnosis was dengue fever but the non-structural antigen 1 (NS1) examination was negative. The patient was later diagnosed with fever paraneoplastic syndrome/bacterial infection.

Patients also experience elevated levels of the enzyme transaminase and dyspnea. X-rays showed minimal pleural...
efusion on the left with suspected metastases. The USO-FZ laparotomy plan was postponed because the patient's condition was unstable. Laparotomy was performed on 4/5/2020, when the surgery obtained the internal genitalia, the uterus was large and solid consistency, and it appeared that a solid tumor originating from the right ovary, size 10x10 cm, mobile. The left ovary appeared to be 4x5 cm in size, mobile, ascites (+). It was decided to do a dextralpingo-oophorectomy with frozen section technique with the result that a malignancy tends to be germ cell tumors. The patient was subsequently diagnosed with Stage IIIA ovarian carcinoma post dextralpingo-oophorectomy and omentectomy.

In this case, the patient was not subjected to a fine-needle aspiration biopsy (FNAB) because the ultrasound examination found a cystic mass in the adnexa, making it impossible to perform FNAB. The next method of surgery is a frozen section, after surgery the patient is diagnosed with Stage III ovarian carcinoma which tends to be germ cell tumors. Pathology Anatomy results out 9 days postoperatively showed a diffuse large B cell lymphoma. Then the patient was transferred to the hematology division and chemotherapy was planned but had to wait for the surgical wound to dry. Unfortunately, the condition had worsening such as fever rising and falling, severe fatigue, acute bronchitis, and bilateral pleural effusions at least as suspected as metastatic NHL diffuse large B cell lymphoma Stage III, and thrombocytopenia (16.93). On the 20th day after laparotomy, the patient lost consciousness and was pronounced dead.

3. Discussion

Diagnosis of ovarian lymphoma can be very difficult, as this disease can closely resemble a gynecological malignancy such as ovarian cancer. In the early stages of lymphoma of the genital organs, the patient tends to be asymptomatic, the patient usually comes to the doctor only when the patient has developed symptoms of abdominal pain, abnormal vaginal discharge, abnormal vaginal bleeding, and flatulence. Patients tend to go to a gynecologist more than a hematologist because there is much controversy in the histogenesis of POL. The ovaries contain only a small amount of lymphatic tissue. The ovaries normally do have B-cell and T-cell lymphocytes in cortical granulomas and few lymphocytes are also found throughout the ovarian stroma and in ovarian follicles and corpora lutea which can be sources of NHL.

Another thing that complicates the preoperative diagnosis of ovarian lymphoma is the absence of radiological features that differentiate NHL from other ovarian malignancies. Some cases show computerized tomography (CT) scan results in the form of hypodense lesions with light contrast enhancement, whereas ultrasonography (USG) presents a nonspecific picture with a hypoechoic and homogeneous structure. MRI depicts a homogeneous mass with hypointense. If ascites are absent and there is a homogeneous bilateral tumor on the ovary, the most likely diagnosis is ovarian lymphoma. Laboratory examinations that can help diagnose ovarian lymphoma are serum levels of carcinoembryonic antigen (CEA), cancer antigen 19-9, AFP, β-HCG which are usually normal in patients with ovarian lymphoma and are useful for differentiating it from other ovarian malignancies. Some literature also states that laboratory testing for human immunodeficiency virus (HIV) and Epstein-Barr virus (EBV) infection is also recommended. Besides, evaluation of bone marrow aspirated cerebrospinal fluid and positron emission tomography are useful to clarify the diagnosis.8

Surgery is not the treatment of choice in patients with ovarian lymphoma. However, surgical intervention plays an important role in the diagnostic process providing clinical, staging, and immunohistological examination information. It is therefore not clear whether surgery should be performed given the effectiveness of chemotherapy and the relatively high mortality and morbidity rates associated with surgery however, surgery may be indicated if there are acute abdominal complications.8

Preoperative diagnostic imaging and intraoperative frozen section results are not always conclusive. This uncertainty could result in patients undergoing unnecessary tumor debulking. If the diagnosis of NHL is known before surgery, surgery can be avoided and treated conservatively. Staging operation and cytoreduction are not indicated in patients with a diagnosis of pelvic NHL, because these patients are very responsive to chemotherapy. Biopsy of suspicious lesions before surgery can help make a diagnosis.2

NHL tumors that grow rapidly are very responsive to chemotherapy. The current first-line therapy is Cyclophosphamide, Doxorubicin, Vincristine, Prednisone (CHOP) combined with Rituximab for at least 3 cycles and 6 for severe disease. This chemotherapy regimen, when combined with radiation therapy, results in a cure rate of approximately 60-70%. Lymphoma, which has a slower growth pattern, does not require aggressive treatment such as R-CHOP. In patients with indolent NHL or mantle-cell lymphoma, Bendamustine-Rituximab treatment increased response rates and decreased toxicity when compared to R-CHOP.2 Patients with ovarian lymphoma mostly diagnosed after surgery will be treated with chemotherapy while
radiotherapy is optional. The chemotherapy protocol used in diffuse large B-cells is the standard R-CHOP regimen.

The patient initially underwent surgery with a frozen section, which is the best management method at our center at Sanglah General Hospital. However, the results of anatomic pathology showed that the ovaries were DLBCL type, so the next appropriate therapy was chemotherapy. The report, in this case, indicated that the patient also planned to undergo chemotherapy when the diagnosis of NHL ovaries was upright, however, there was a delay in diagnosis due to atypical symptoms so that chemotherapy had not been carried out because the patient's condition was getting worse. Based on a literature review of 21 studies approximately 60% of primary ovarian lymphoma patients underwent surgery after an ovarian tumor was detected. About 90% of patients underwent chemotherapy. Bilateral ovary removal in young patients appears to be more dangerous, but chemotherapy can also cause infertility in these patients.8

In this case report, the patient's prognosis was poor where the patient died 20 days after surgery or 7 days after the diagnosis of ovarian NHL was confirmed by pathological anatomical examination, with the direct cause of death being acute respiratory distress syndrome with hospital-acquired pneumonia and pulmonary metastases. Once the incisional or excisional biopsy of Non-Hodgkin's lymphoma has been confirmed, a complete examination should be performed to determine staging which includes a full-body CT scan and/or positron emission tomography (PET) scan followed by a bone marrow biopsy. PET scanning is now commonly used in staging, detecting recurrences, and monitoring treatment. Other tumor markers, such as CA-125 levels, may also be useful. An increase in CA-125 (concentration above 35 U/mL) at the time of diagnosis of NHL has been associated with a decrease in the 5-year survival rate. Higher levels of CA-125 were associated with advanced conditions, extranodal disease, large tumors, and occurrence of B symptoms, pleural and peritoneal effusions, bone marrow involvement, high serum LDH levels, high serum beta2 microglobulin, and poor response to treatment. In this case, it has not been done, so the staging determination to determine the prognosis is not optimal.

Primary ovarian lymphoma or PONHL has a poor prognosis with a range from 0% to 36% survival for 3 years. Often the prognosis of ovarian lymphoma is worse than nodal lymphoma because of late or inaccurate diagnosis. The best treatment option is chemotherapy. Clinicians should be aware of this rare presentation to avoid radical surgery, which is unnecessary.5 Early clinical manifestation of occult nodal lymphoma as an ovarian mass is known to have a poor outcome with 5-year survival ranging from 7% to 38%. Most people with ovarian lymphoma experience the morbidity associated with surgery as a result of the uncertainty of the preoperative diagnosis. There is a question of whether surgery increases morbidity or mortality, but there is a lack of data due to the rarity of PONHL cases. Recent evidence shows late diagnosis due to non-specific symptoms, tumor type, and grade histologically as a poor prognostic factor.5

Clinical markers associated with poor prognosis of DLBCL include poor performance status at diagnosis of the Eastern Cooperative Oncology Group (ECOG), advanced tumor stage (Ann Arbor stage III-IV), high LDH, and involvement of an extranodal gland. In this case, the patient was diagnosed with NHL Diffuse large B cell Stage IIIIE lymphoma, resulting in a poor prognosis. Another important prognosis factor is the patient's age because it is related to the patient's ability to tolerate chemotherapy.14 The patient, in this case, a 31-year-old, is relatively young, so the ability to tolerate chemotherapy is good enough, however, unfortunately before chemotherapy, the patient's condition worsened until she was pronounced dead.

4. Conclusion

Primary ovarian NHL is a difficult case to diagnose because it can be mistaken for other genital malignancies. Diagnosis is a crucial step in handling this case. The need for a complete preoperative examination such as tumor marker CA-125, including FNAB on the ovary, especially in patients with adnexal tumors who have risk factors for NHL and show NHL-specific symptoms. If a bilateral, solid, homogeneous adnexal mass is found accompanied by specific symptoms of NHL B cells such as fever, severe fatigue, night sweats, and weight loss, it is necessary to consider ovarian NHL as the main differential diagnosis. Once the diagnosis has been established it is obligatory to immediately carry out a thorough examination to determine the staging and type of primary or secondary ovarian lymphoma that can help determine the prognosis.

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6. Authors’ Contribution

SEJ is obstetrics and gynecology resident, while IGSW is her supervisor. Both SEJ and IGSW have treated the patients. SEJ wrote the manuscript. IGSW, IGPM, KFM, and IWM helped to revise and review the manuscript. All authors have read and approved the final version of this manuscript.

7. Conflict of Interest

The authors declare that they have no conflict of interest.
Figure 1: Upper lower abdominal ultrasound. On these images above found: a solid mass with multiple internal cystic components on the right adnexa, measuring about 8.6 x 6.1 cm, suggesting a mass of the right ovary; para-aortic multiple lymphadenopathies; bilateral pleural effusions; suspected accessory splenic nodule; normal liver morphology, Gallbladder, pancreas, kidney right and left, bladder no visible abnormality.

Figure 2: Rontgen Thorax PA of the patient showed Bronchitis and minimal pleuraeffusion on the left side (April 28th, 2020).

Figure 3: A laparotomy images showing ovarian tumor

References


