Received: 2012.01.07
Accepted: 2012.05.10
Published: 2012.06.05

Ovary involvement of diffuse large B-cell lymphoma

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Summary

Background: Primary ovarian non-Hodgkin's lymphoma (PONHL) is an uncommon entity; its pathology is usually diffuse large B cell lymphoma (DLBCL).

Case Reports: We report 3 cases of ovary involvement of DLBCL, 1 of which rapidly developed to central nervous system involvement. Diagnosis and subsequent treatment are discussed and the literature on the origin, epidemiology, clinical presentation, diagnosis, treatment and prognosis of ovary lymphoma are reviewed. All patients were diagnosed as having DLBCL after ovary biopsy, and were subsequently given regular chemotherapy. Two of them obtained remission and 1 of them had central nervous system involvement.

Conclusions: Ovary involvement of DLBCL is rare; prognosis is related to the overall clinical manifestation and some serum biomarkers. Diagnosis is established by ovary biopsy. Inaccurate or delayed diagnosis is often due to the lesions presenting as a mass resembling ovary cancer and may lead to poor outcome. Treatment regimen mainly consists of chemotherapy (CHOP) associated with rituximab. Intrathecal chemotherapy may play an important role in prevention of central nervous system involvement.

key words: ovary • DLBCL-lymphoma • central nervous system (CNS) • intrathecal chemotherapy

Full-text PDF: http://www.amjcaserep.com/fulltxt.php?ICID=882997

Word count: 1297
Tables: –
Figures: –
References: 16

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Background

Ovary involvement is usually a manifestation of disseminated lymphoma. PONHL is an uncommon entity because the ovary lacks lymphatic tissues. It may be misdiagnosed as ovary epithelial cancer, and the exact mechanism is unclear. It does not show a specific manifestation; common symptoms include uncertain abdominal pain, fever, night sweats, and weight loss. The signs include lower abdominal mass. The pathology of PONHL is usually diffuse large B cell lymphoma. Here we describe 3 cases of PONHL, 1 of which rapidly developed to central nervous system (CNS) involvement.

Case Reports

Clinical case 1

A 57-year-old woman was admitted to our hospital with right lower limb and left waist pain and weight loss (4 kg) of 2 months duration. She had no fever or night sweats. A physical examination revealed abdominopelvic pain and no palpable masses. There was no superficial lymphadenopathy. Computed tomography (CT) showed multiple masses at pelvis and retroperitoneum, and no lymphadenopathy was found. A bilateral adnexectomy with omentectomy, appendectomy, peritoneal cytology, and peritoneal biopsy were performed. The left ovary mass was 13.5×9.5 cm and the right mass was 13.0×7.5 cm. Ovary biopsy showed CD20(+), Ki67 (more than50%+), CD3(–), CD23(–), CD5(–), CD10(–), CD79A(–), Bcl-2(–), Bcl-6(–), TdT(–), EMA(–), CgANse(–) and CK(–). Bone marrow cells analysis showed lymphoma cells accounted for 13.6%. Serum lactate dehydrogenase was 236U/L (125–243 U/L); serum CA-199 was 44.73 U/L (0–35 U/L); and serum β_2-microglobin was 4.1 mg/L (0.7–1.8 mg/L). Serology for human immunodeficiency virus, hepatitis C virus, and hepatitis B virus was negative. The patient was diagnosed with non-Hodgkin's lymphoma (diffuse large B-cell phenotype) and was assessed as stage III according to the Ann Arbor system. The international prognosis index (IPI) score was 2. She has received 6-course CHOP regimen (cyclophosphamide, daunorubicin, vincristine and dexamethasone every 21days) and 6-course intrathecal chemotherapy to prevent CNS involvement.

Clinical case 2

A 31-year-old woman with HBsAg-positivity was admitted to our hospital with persistent right lower abdominal pain of 1 day duration. She had no fever, night sweats or weight loss. A physical examination revealed right lower abdominal tenderness and no palpable masses. There was no superficial lymphadenopathy. CT showed multiple lymphadenopathies at the pelvis and retroperitoneum. A right oothecectomy was performed. The right ovary mass was 13cm×11cm. Ovary biopsy showed CD20(+), CD3(–), Ki67 (about 80%+), MuM-1(+), EMA(–), CD30(–), Bc1-6(–), CD10(–), CK(–), Inhibin(–), and CD99(–). Bone marrow cells analysis was normal. Serum lactate dehydrogenase was 241U/L (125–243 U/L); serum CA-125 was 79.46 U/L (0–35 U/L); and serum β_2-microglobin was 1.7 mg/L (0.7–1.8 mg/L). The patient was diagnosed with non-Hodgkin's lymphoma (diffuse large B cell phenotype) and the stage was assessed according to the Ann Arbor system. The IPI score was 1. She has received 6-course R-CHOP regimen (rituximab, cyclophosphamide, daunorubicin, vincristine and dexamethasone every 21days) and 6-course intrathecal chemotherapy to prevent CNS involvement.

Clinical case 3

A 43-year-old woman was admitted to our hospital with abdominal pain and flatulence of 20 days duration. She had no fever, night sweats or weight loss. She had an operation of uterus and bilateral appendices. There was no superficial lymphadenopathy. Positron Emission Tomography/Computed Tomography (PET-CT) showed multiple lymphadenopathies with high 18-FDG activity. Bilateral adnexectomy with omentectomy was performed. The right ovary mass was 3.5×2.5×1 cm. Ovary biopsy showed CD3(scatter +), CD20(+), CK(–),EMA(–), CD15(–), CD30(–), and CD45(–). Bone marrow cells analysis was normal. Serum lactate dehydrogenase was 864 U/L (125–243 U/L); serum CA-125 was 139.4 U/L (0–35 U/L); and serum β_2-microglobin was 5.3 mg/L (0.7–1.8 mg/L). Serology for human immunodeficiency virus, hepatitis C virus, and hepatitis B virus was negative. The patient was diagnosed with non-Hodgkin's lymphoma (diffuse large B cell phenotype) and was assessed at stage IV according to the Ann Arbor system. The IPI score was 3. She received 3-course E-CHOP regimen (etoposide, cyclophosphamide,daunorubicin, vincristine and dexamethasone), 1 course ESHAP (etoposide, cisplatin, methylprednisolone, and cytarabine). She did not receive regular intrathecal chemotherapy. Three months after diagnosis she suffered headache, nausea without vomiting, and hypesthesia with numbness of her fingertips. A physical examination revealed the left eyelid could not close completely, the corner of her mouth was oblique to the right side, and her face wrinkles had obviously decreased. After a course ESHAP, the patient died from infective shock.

Discussion

Involvement of the ovary is frequently secondary to disseminated malignant lymphoma, with an incidence of 7–26% [1]. PONHL is an uncommon entity, accounting for 0.5% of all non-Hodgkin's lymphomas and 1.5% of all ovarian neoplasms[2]. Diffuse large B cell type accounts for about 20% of PONHL according to a single-center study[3].This may be due to lack of lymphoid tissue within the ovary. It has been suggested that the PONHL originates from lymphocytes in the ovaries, surrounding blood vessels at the hilum and related to the corpus luteum. Most authors consider PONHL as a local involvement of a systemic disease. It should be differentiated from advanced epithelial carcinoma, which usually presents elevated tumor markers and ascites. Chemotherapy, but not radical surgery, is an optimal treatment [4]; thus, accurate diagnosis is critical to avoid unnecessary operation.

Fox et al proposed the following criteria for the diagnosis of PONHL [5]: (1) At the time of diagnosis, the lymphoma is clinically confined to the ovary and a complete investigation fails to reveal evidence of lymphoma elsewhere. However, an ovarian lymphoma can still be considered as primary if it has spread to immediately adjacent lymph nodes or if it has directly spread to infiltrate immediately adjacent structures. (2) The peripheral blood and bone marrow should not contain any abnormal cells. (3) If further lymphomatous

lesions occur at sites remote from the ovary, then at least several months should have elapsed between the appearance of the ovarian and extraovarian lesions. According to these strict criteria, only Case 2 in our report can be diagnosed as PONHL.

The survival of PONHL ranges widely from 0% to 36%,with an average survival time of less than 3 years, according to different reports [2,6]. Prognosis of ovarian lymphomas is often poorer than nodal lymphomas due to inaccurate or delayed diagnosis [7]. Unilateral ovarian involvement and focal involvement of the ovary may be indicators of good prognosis, while rapid growth of pelvic mass, severe systemic symptoms, bilateral ovarian tumors, and advanced stage may be indicative of poor prognosis [8,9]. In our report, only Case 2 was unilateral ovarian involvement.

Clinical stage, modality of onset, histological type and IPI index are also considered as useful prognostic factors [10,11]. There is no standard regimen for ovary involvement of NHL, including PONHL, due to its rarity. The best option should be adapted to the specific histology [4,12]. CD20(+) could be an indicator for use of rituximab and Case 2 of our report demonstrates that rituximab combined with CHOP may be well-tolerated and result in satisfactory response.

Due to its rarity, central nervous system involvement of ovary lymphoma is seldom reported. Our Case 3 unfortunately developed to CNS involvement and soon died from relapse, while our other 2 cases did not suffer from CNS involvement, which may benefit from regular intrathecal chemotherapy. Jeremy et al showed that intravenous methotrexate can be safely administered concurrently with R-CHOP and is associated with a low risk of CNS recurrence in high-risk DLBCL [13–15]; however, they did not study ovarian DLBCL.

Conclusions

Although rituximab can salvage the patient from lymphoma, new clinical research[16] showed that rituximab could not prevent lymphoma patients from developing CNS involvement. As an adrenal tissue, the ovary is prone to CNS involvement and we recommend regular preventive intrathecal chemotherapy, which the National Comprehensive Cancer Network (NNCN) guideline does not address. Research leading to a more effective strategy is urgently needed.

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