Case Report

Ovarian Diffuse Large B-cell Lymphoma Initially Suspected Dysgerminoma Managed by Laparoscopic Staging Surgery

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Abstract

Ovarian diffuse large B-cell lymphoma (DLBCL) is rare. DLBCL is a complex type of lymphoma. The ovarian DLBCL usually harbor a favorable prognosis. We report a case of ovarian DLBCL that presented as an ovarian mass with lower abdominal pain and was managed using laparoscopic staging surgery. A 29-year-old female (gravida 2, para 0, abortion 2) with a history of polycystic ovarian syndrome with irregular medication control visited our clinic due to lower abdominal pain. Transvaginal ultrasound revealed a heterogeneous, septated mass over the left adnexa with a diameter of approximately 6 cm × 8 cm. The tumor marker CA 19-9 was elevated (65.77 IU/mL); CA125 and carcinoembryonic antigen were not elevated. Laparoscopic surgery with left salpingo-oophorectomy was first performed. Frozen section indicated dysgerminoma. Then, we continued staging surgery through bilateral pelvic lymph node dissection, para-aortic lymph node dissection, omentectomy, right ovary and peritoneum biopsy, and washing cytology. Ovarian tumor and para-aortic lymph nodes were positive for lymphoma. The tumor cells were positive staining for CD20, CD5, ki67, BCL-6, and MUM-1, which was associated with DLBCL. The patient was then consulted for oocyte preservation and referred to hematology for further chemotherapy. In conclusion, an ovarian lymphoma is a rare event. The presence of an enlarged ovarian tumor should raise the suspicion of ovarian lymphoma. To differentiate ovarian lymphoma from dysgerminoma, immunohistochemistry is useful. Fertility preservation should be considered before chemotherapy. Ovarian tissue or oocyte preservation or gonadotropin-releasing hormone agonist injection before chemotherapy can be performed for fertility preservation.

Keywords: B cell, CD20, laparoscopy, lymphoma, ovary

Introduction

Ovarian lymphoma is rare. However, the ovary is a common site that is involved in many hematological cancers.[1] Because the ovary contains no lymphoid tissue, the primary occurrence of lymphoma in the ovaries has long been debated.[2] Thus, ovarian lymphoma could be a primary or secondary occurrence and is incidentally found after a workup for abdominal mass.[3]

Diffuse large B-cell lymphoma (DLBCL) is a clinicopathological heterogeneous lymphoma group. DLBCL can be divided into activated B-cell-like (ABC) and germinal center B-cell-like DLBCL.[4] The 5 years' survival is 70% in ovarian lymphoma.[5]

Article History:
Submitted: 13 August 2019
Revised: 25 November 2019
Accepted: 19 February 2020
Published: 9 May 2020

Access this article online

Quick Response Code:

Website: www.e-gmit.com

DOI: 10.4103/GMIT.GMIT_79_19

We report a rare case of ovarian DLBCL that presented as an ovarian mass with lower abdominal pain and was managed using laparoscopic staging surgery initially diagnosed as dysgerminoma at the frozen section. We have obtained informed consent from the patient and got the approval letter from the Research Ethical Committee of our hospital (CR108-04).

Case Report

A 29-year-old female (gravida 2, para 0, abortion 2) had a history of polycystic ovary syndrome with irregular

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How to cite this article: Li PC, Lim PQ, Hsu YH, Ding DC. Ovarian diffuse large B-cell lymphoma initially suspected dysgerminoma managed by laparoscopic staging surgery. Gynecol Minim Invasive Ther 2020;9:162-5.

medication control presented to our outpatient department due to lower abdominal pain. No dizziness or sweating was noted. Per vaginal examination revealed a mass in the left adnexal area. Transvaginal ultrasound revealed a heterogeneous, septated mass over the left adnexa with approximate dimensions of 7.3 cm × 6.1 cm [Figure 1a]. Laboratory data showed unremarkable results. The tumor marker CA19-9 was elevated (65.77 IU/mL); carcinoembryonic antigen and CA125 were not elevated (1.0 ng/mL and 9.1 IU/mL). An abdominal computed tomography (CT) scan showed a left pelvic mass with heterogeneous content [Figure 1b]. Lymphadenopathy or splenomegaly was not noted. Ovarian germ cell tumor was first suspected.

Laparoscopy

Due to the possibility of ovarian germ cell malignancy, laparoscopic surgery with left salpingo-oophorectomy (LSO) was first planned and performed [Figure 2]. We made one single port (one 11 mm and one 5 mm trocars inserted into two fingers of the glove) and two accessory ports with a 5 mm trocar at the bilateral abdominal region. We did LSO by Ligasure electrocauterization. The left adnexa was then safely placed into the tissue bag. Then, we removed the tissue bag through a single port and did contained-morcellation in the bag.[6,7] Frozen section of the tumor reported dysgerminoma. Then, we continued staging surgery through bilateral pelvic lymph node dissection, para-aortic lymph node dissection, omentectomy, right ovary biopsy, peritoneal random biopsy over bilateral gutters and pelvic cavity, and washing cytology.

Pathology

A frozen section of the ovarian tumor was first requested intraoperatively. A left ovarian tumor of approximately 8 cm in diameter with an irregular shape was noted. Grossly, the tissue was elastic and yellowish. Extensive necrosis and several viable hypercellular regions were noted. The surgeon thought the tumor may be a dysgerminoma. The pathologist confirmed the diagnosis of dysgerminoma according to the histology showed large open nuclei and fibroconnective tissue septa among the tissue.

At permanent sections, microscopically, the left ovary showed numerous malignant large lymphoid cells [Figure 3a], positive for CD20 (a B-cell marker) [Figure 3b] and a CD3 T-cell-rich background [Figure 3c], revealing a T-cell/histiocyte-rich large B-cell (THRLBCL) lymphoma with an activated B-cell subtype. The left fallopian tube, right ovary, left pelvic lymph nodes, and right pelvic lymph nodes were negative for malignancy. The para-aortic lymph nodes were also positive for lymphoma. The omentum showed one calcifying nodule. Other immunohistochemical staining showed that the tumor cells were positive staining for CD5, ki67 (>90%), BCL-6 (15%), and MUM-1 (50%) [Figure 3d] and negative for c-kit, CD10, cyclin D1, SOX-11, and CD30.

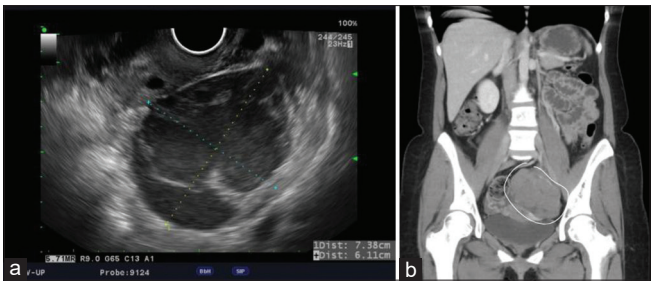

Figure 1: Imaging results of ovarian lymphoma. (a) Ultrasound revealed a left ovarian tumor measuring 7.3 cm × 6.1 cm in diameter. (b) Coronal view of abdominal computed tomography revealed a left ovarian tumor (white line)

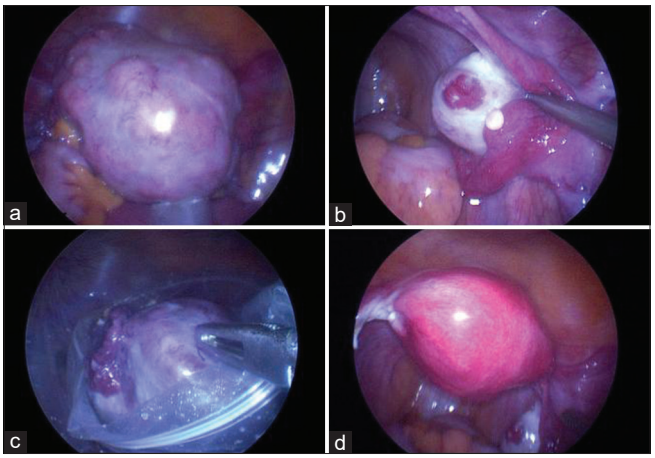

Figure 2: Laparoscopic image of ovarian lymphoma. (a) Left ovarian tumor. (b) Right normal ovary. (c) Cut left adnexa placed to a tissue bag. (d) Uterus

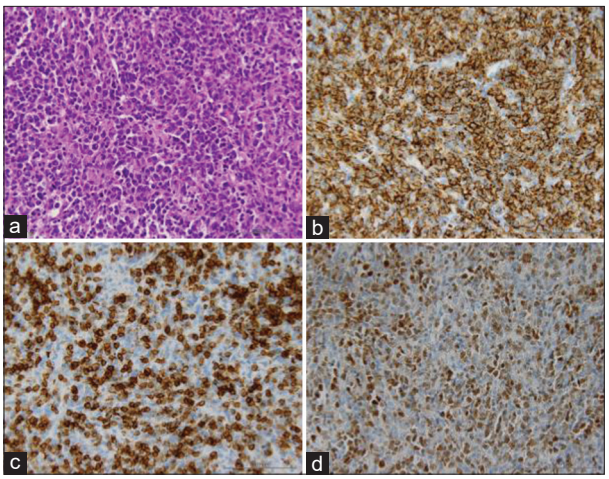

Figure 3: Histopathology and immunohistochemistry of ovarian lymphoma. (a) H and E, (b) CD20, (c) CD3, (d) MUM-1. Scale bar = 100 μm

The patient was then indicated for oocyte preservation and referred to hematology for further chemotherapy.

Discussion

We reported a rare case of ovarian ABC DLBCL. Lymphoma is not a surgical disease. However, when lymphoma occurred in

the ovary of a young female without other lymphoma-related symptoms, it could be regarded as germ-cell malignancy.

Frozen section of ovarian tumor in our case revealed dysgerminoma. The previous report had been shown in histology, lymphoma may look like dysgerminoma due to lymphoma also showed a monotonous cell proliferation with moderate-size nuclei and clear or pale cytoplasm.[8] Septate of connective tissue may increase the similarity. Lymphoma usually surrounds the ovarian stroma as in the dysgerminoma. The nuclei in dysgerminoma are vesicular. However, the lymphoma nuclei are coarsely granular and prominent. CD20 is positive in lymphoma and negative in dysgerminoma.

The ultrasound feature of the dysgerminoma is a solid tumor.[9] However, the tumor, in this case, showed a heterogeneous, septated mass lesion by ultrasound. However, CT scan of this case showed a more solid lesion. It may due to different scan density settings. The tumor markers for germ-cell tumors include CA199, lactate dehydrogenase (LDH), human chorionic gonadotropin, and alpha-fetoprotein (AFP).[10] AFP will be positive in yolk sac tumor (100%), immature teratoma (61.9%), and dysgerminoma (11.8%). CA199 will be elevated in teratomatomatous tumors, including immature teratoma. LDH was linked to dysgerminoma. In our case, due to elevated CA199, immature teratoma was suspected firstly.

The involvement of the ovary in malignant lymphoma is uncommon. Ovarian lymphoma accounts for 0.5% of all cases of non-Hodgkin lymphoma.[11] Lymphoma has a low incidence in the ovary because of the absence of lymphoid tissue in the ovary. Lymphoma usually originates from lymphocytes in the vessels of the hilum or corpus luteum. In the ovary, DLBCL is the most common type, followed by Burkitt lymphoma.[12] THRLBCL is a rare morphological variant of DLBCL and is composed of infiltrating reactive T-cells with predominantly macrophages (histiocytes). The differential diagnosis of solid ovarian mass includes epithelial tumor, teratoma, dysgerminoma, yolk sac tumor, fibrothecoma, granulosa cell tumor, and metastatic tumor.[13]

Ovarian lymphoma can occur at any age but it is most often reported in young women, with a median age of 33–42 years.[14,15] Bilateral involvement has been previously reported in approximately 38%–71% of cases.[15,16] The clinical presentation of ovarian lymphoma includes abdominal pain, abdominal mass, irregular vaginal bleeding, and ascites or pleural effusion. Some patients present with fever, emaciation, fatigue, or night sweats (B symptoms). Physical examination may reveal palpable adenopathy or a liver or spleen infiltration.[17]

Laparoscopic staging for the early stage of ovarian cancer is feasible.[18] A systematic review also showed laparoscopic staging surgery for ovarian cancer showed longer operative time, shorter hospital stay, a short period from surgery to chemotherapy, and equivalent survival than laparotomy.[19] Another report showed 26 women with early-stage ovarian cancer received laparoscopic staging surgery. They concluded that laparoscopic is a valuable treatment for early-stage ovarian cancer.[20] In our case, we thought the ovarian tumor was apparently an early stage. We, therefore, performed laparoscopic staging surgery for her. The tumor was safely contained with tissue bag and retrieved by manual morcellation through a single-port setting. Although the case is not a germ-cell malignancy, it implies that laparoscopic staging surgery might be feasible for early-stage ovarian cancer.

The first-line treatment of DLBCL is the rituximab, cyclophosphamide, doxorubicine, vincristine, prednisone (R-CHOP) regimen. Because our patient was a 29-year-old young female, fertility preservation was a concern. Treatments following protocols that contain alkylating agents (cyclophosphamide, vincristine, and prednisolone) can induce premature ovarian insufficiency. Some methods can be used to preserve fertility such as cotreatment with a gonadotropin-releasing hormone agonist (GnRH-a), cryopreservation of oocytes or embryos, and cryopreservation of the ovarian tissue. Cotreatment with GnRH-a is an easy, low-cost method but with an unknown protective effect. Cryopreservation of oocytes or embryos might fail to provide enough time for the patient to undergo an *in vitro* fertilization cycle. Ovarian tissue cryopreservation can often be performed on very short notice is suitable for young prepubertal girls and offers a high chance of reestablishing the ovarian function (endogenous hormone production and return of menstrual cycles).

Primary ovarian lymphoma typically has favorable outcomes. The 5-year overall survival of primary ovarian DLBCL was 70.0%.[16]

If early-stage ovarian cancer patient desires future fertility, unilateral salpingo-oophorectomy with comprehensive surgical staging should be performed.[21] In germ-cell tumor cases, nature fertility could be maintained. Only 12% of patients ask for assisted reproductive technology (ART). ART includes oocyte or embryo cryopreservation.[22] Oocyte cryopreservation is more challenging than embryo preservation. The procedure of oocyte cryopreservation requires 2 weeks of controlled ovarian stimulation (COS) and pick up the mature oocytes after follicles maturation. COS is considered safe for cancer patients with delayed 2 weeks to initiate treatment.[23] The methods of oocyte cryopreservation include slow freezing (controlled-rate cryopreservation) and vitrification. The pregnancy rate was higher in oocyte

cryopreservation with vitrification than slow freezing.[24] Our patient did not get married, therefore, she chose oocyte cryopreservation.

Conclusion

An ovarian lymphoma is a rare event. The presence of an enlarged ovarian tumor should be suspected for ovarian lymphoma. To differentiate ovarian lymphoma from dysgerminoma, immunohistochemistry is useful. Fertility preservation should be considered before chemotherapy. Ovarian tissue or oocyte preservation or GnRH agonist injection should be considered before chemotherapy for fertility preservation.

Ethical approval

We have obtained informed consent from the patient and got the approval letter from the Research Ethical Committee of our hospital (CR108-04).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ferry JA, Young RH. Malignant lymphoma of the genitourinary tract. Curr Diagn Pathol 1997;4:145-69.
2. Crasta JA, Vallikad E. Ovarian lymphoma. Indian J Med Paediatr Oncol 2009;30:28-30.
3. Osborne BM, Robboy SJ. Lymphomas or leukemia presenting as ovarian tumors. An analysis of 42 cases. Cancer 1983;52:1933-43.
4. Takeuchi T, Yamaguchi M, Kobayashi K, Miyazaki K, Tawara I, Imai H, *et al*. MYD88, CD79B, and CARD11 gene mutations in CD5-positive diffuse large B-cell lymphoma. Cancer 2017;123:1166-73.
5. Miyazaki K, Yamaguchi M, Suzuki R, Kobayashi Y, Maeshima AM, Niitsu N, *et al*. CD5-positive diffuse large B-cell lymphoma: A retrospective study in 337 patients treated by chemotherapy with or without rituximab. Ann Oncol 2011;22:1601-7.
6. Wu MY, Ding DC, Chu TY, Hong MK. "Contain before transection, contain before manual morcellation" with a tissue pouch in laparoendoscopic single-site subtotal hysterectomy. Gynecol Minim Invasive Ther 2016;5:178-81.
7. Ding DC, Hong MK, Chu TY, Chang YH, Liu HW. Robotic single-site supracervical hysterectomy with manual morcellation: Preliminary experience. World J Clin Cases 2017;5:172-7.
8. Wang Q, Rodriguez R, Marcus JZ, Podolsky L, Campbell D, Heller D. Pitfalls of frozen section in gynecological pathology: A rare case of ovarian lymphoma in an HIV-positive woman resembling dysgerminoma on frozen Section. Int J Surg Pathol 2019;27:387-9.
9. Guerriero S, Testa AC, Timmerman D, Van Holsbeke C, Ajossa S, Fischerova D, *et al*. Imaging of gynecological disease (6): Clinical and ultrasound characteristics of ovarian dysgerminoma. Ultrasound Obstet Gynecol 2011;37:596-602.
10. Kawai M, Kano T, Kikkawa F, Morikawa Y, Oguchi H, Nakashima N, *et al*. Seven tumor markers in benign and malignant germ cell tumors of the ovary. Gynecol Oncol 1992;45:248-53.
11. Kumar N, Kumar R, Bera A, Srinivasan R, Sharma SC. Primary ovarian lymphoma: A case report and review of literature. J Obstet Gynaecol India 2014;64:65-7.
12. Onyiuke I, Kirby AB, McCarthy S. Primary gynecologic lymphoma: Imaging findings. AJR Am J Roentgenol 2013;201:W648-55.
13. Jung SE, Lee JM, Rha SE, Byun JY, Jung JI, Hahn ST. CT and MR imaging of ovarian tumors with emphasis on differential diagnosis. Radiographics 2002;22:1305-25.
14. Monterroso V, Jaffe ES, Merino MJ, Medeiros LJ. Malignant lymphomas involving the ovary. A clinicopathologic analysis of 39 cases. Am J Surg Pathol 1993;17:154-70.
15. Dimopoulos MA, Daliani D, Pugh W, Gershenson D, Cabanillas F, Sarris AH. Primary ovarian non-Hodgkin's lymphoma: Outcome after treatment with combination chemotherapy. Gynecol Oncol 1997;64:446-50.
16. Yun J, Kim SJ, Won JH, Choi CW, Eom HS, Kim JS, *et al*. Clinical features and prognostic relevance of ovarian involvement in non-Hodgkin's lymphoma: A Consortium for improving survival of lymphoma (CISL) report. Leuk Res 2010;34:1175-9.
17. Türken A, Ciftci AO, Akçören Z, Köseoglu V, Akata D, Senocak ME. Primary ovarian lymphoma in an infant: Report of a case. Surg Today 2000;30:305-7.
18. Nezhat FR, Ezzati M, Chuang L, Shamshirsaz AA, Rahaman J, Gretz H. Laparoscopic management of early ovarian and fallopian tube cancers: Surgical and survival outcome. Am J Obstet Gynecol 2009;200:83.e1-6.
19. Bogani G, Borghi C, Leone Roberti Maggiore U, Ditto A, Signorelli M, Martinelli F, *et al*. Minimally invasive surgical staging in early-stage ovarian carcinoma: A systematic review and meta-analysis. J Minim Invasive Gynecol 2017;24:552-62.
20. Ghezzi F, Cromi A, Siesto G, Serati M, Zaffaroni E, Bolis P. Laparoscopy staging of early ovarian cancer: Our experience and review of the literature. Int J Gynecol Cancer 2009;19 Suppl 2:S7-13.
21. Johansen G, Dahm-Kähler P, Staf C, Flöter Rådestad A, Rodriguez-Wallberg KA. Fertility-sparing surgery for treatment of non-epithelial ovarian cancer: Oncological and reproductive outcomes in a prospective nationwide population-based cohort study. Gynecol Oncol 2019;155:287-93.
22. Massarotti C, Scaruffi P, Lambertini M, Remorgida V, Del Mastro L, Anserini P. State of the art on oocyte cryopreservation in female cancer patients: A critical review of the literature. Cancer Treat Rev 2017;57:50-7.
23. Lambertini M, Del Mastro L, Pescio MC, Andersen CY, Azim HA Jr., Peccatori FA, *et al*. Cancer and fertility preservation: International recommendations from an expert meeting. BMC Med 2016;14:1.
24. Levi Setti PE, Porcu E, Patrizio P, Vigiliano V, de Luca R, d'Aloja P, *et al*. Human oocyte cryopreservation with slow freezing versus vitrification. Results from the National Italian Registry data, 2007-2011. Fertil Steril 2014;102:90-500.