CASE REPORT

Case of primary bilateral diffuse large B-cell lymphoma of the ovary with plasmablastic features in an HIV-negative female patient

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SUMMARY

A 37-year-old woman from Puerto Rico presented to our clinic with symptoms of an abdominal distension progressively worsening over 1 year. A CT of an abdomen and pelvis with contrast was performed and revealed bilateral large heterogeneous pelvic adnexal masses with large ascites and right pleural effusion. Tumour markers CA 125 was 766 U/mL and lactate dehydrogenase was 654 U/L. She underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy with pelvic lymph node dissection and partial omentectomy. Pathology of ovarian masses revealed a diffuse large B-cell lymphoma. The staging work-up was negative, which pointed towards the diagnosis of primary ovarian lymphoma. The patient completed 8 cycles of cyclophosphamide, doxorubicin, vincristine, prednisolone chemotherapy. After 18 months of chemotherapy completion, she remains in remission.

BACKGROUND

Primary ovarian diffuse large B-cell lymphoma (DLBCL) has been described as a very rare entity accounting for <1% of cases in the literature. There are very few case reports of non-Hodgkin's lymphoma (NHL) presenting as unilateral primary ovarian lymphomas but reports describing bilateral involvement are extremely seldom. Here, we present a unique case of bilateral primary ovarian DLBCL with plasmablastic features in an HIV-negative female patient.

CASE PRESENTATION

A 37-year-old woman gravida 9, para 6, was found to have abdominal distension during an office visit. She did not report any fever, chills, night sweats, difficulty breathing or weight loss. Her medical history was remarkable for iron deficiency anaemia. Her medications included multivitamins and iron. She is a smoker since the past 10 years. She denied alcohol or substance use. She had a dilation and curettage for retained placenta 2 years ago and two miscarriages. Her family history is significant for lung cancer in her mother. Her physical examination was normal except for abdominal distension.

INVESTIGATIONS

Her laboratory evaluation showed haemoglobin of 11 g/dL, leucocytosis of 13 600/mL and a neutrophil predominance of 79.1%. Her liver and kidney function tests were normal. Her hepatitis panel was negative. Her HIV test was negative. Her CA 125

was elevated at 766 U/mL (<35 U/mL) along with lactate dehydrogenase at 654 U/L (100–200 U/L).

The chest X-ray showed right pleural effusion without infiltrates. A CT of her chest, abdomen and pelvis with contrast revealed large right pleural effusion along with bilateral large heterogeneous adnexal masses measuring 8.4×7.5×11.3 cm on the right and 7.0×7.2×7.0 cm on the left with prominent bilateral inguinal lymph nodes and scattered shotty para-aortic lymph nodes without frank lymphadenopathy (figure 1).

The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy along with partial omentectomy and pelvic lymph node dissection (figure 2). The frozen section was suggestive of lymphoma. The peritoneum, liver and other adjacent organs were not involved macroscopically. The definite pathological diagnosis revealed DLBCL with plasmablastic features (figures 3–5). Immunoprofile studies revealed that the cells were positive for CD56, BCL2, CD43 and CD79 and negative for CD20, PAX-5, CD3, CD4, BCL-6, P53, LCA/CD45 and HHV-8. The further systemic work-up for lymphoma included bone marrow biopsy, whole body positron emission tomography (PET), cerebrospinal fluid (CSF) analysis and peripheral blood smear. Bone marrow biopsy showed normocellular marrow with trilineage maturation with atypical plasmacytoid cells but was not conclusive for neoplastic cellular infiltration. PET CT performed after surgery did not show any evidence of hypermetabolic foci in other locations besides postsurgical changes, and CSF analysis did not have any evidence of malignant infiltration.

Figure 1 CT scan of the abdomen and pelvis showing bilateral large heterogeneous adnexal masses.

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Figure 2 A laparoscopic picture showing bilateral abdominal tumours and a thickened omentum.

Figure 3 Diffuse large B-cell lymphoma with plasmablastic features showing a 'starry sky' pattern (H&E stain, low magnification ×100).

Pleural fluid analysis was negative for malignant cells. With the above work-up, the definite diagnosis of primary bilateral DLBCL of ovary stage IVB was made.

DIFFERENTIAL DIAGNOSIS

The diagnosis of ovarian carcinoma was an important differential that was considered in this patient as the differentiation from lymphoma clinically and radiologically is challenging.

TREATMENT

Once the definitive diagnosis of primary ovarian DLBCL was made, the patient was treated with eight cycles of cyclophosphamide, doxorubicin, vincristine, prednisolone chemotherapy. Rituximab was not administered as CD20 was negative.

OUTCOME AND FOLLOW-UP

After completion of chemotherapy and at a 1-year interval, she underwent PET CT without any evidence of hypermetabolic foci. She also underwent a CT scan of the chest, abdomen and pelvis 18 months after completion of chemotherapy which did not reveal any recurrence. Thus, she remained in remission after 18 months of treatment completion.

Figure 4 Diffuse large B-cell lymphoma with plasmablastic features. The tumour cells are large, pleomorphic with prominent nucleoli and mitotically active (H&E stain, high power ×400).

Figure 5 The tumour cells are strongly immunoreactive to CD79a (immunohistochemical stain).

DISCUSSION

Incidence of NHL has been increasing for the past few decades. It has reached a plateau in the past 20 years. DLBCL accounts for 40% of total NHL. The CD20 negative plasmablastic variant of DLBCL has been described as a rapidly progressive tumour, almost exclusively involving the jaw and oral mucosa.¹ It has been described in the literature that plasmablastic lymphoma shows an excessive predilection for male gender, HIV infection¹ and other immunodeficiency conditions. Note that our patient is female and does not have HIV.

As the disease progresses, DLBCLs involve extranodal sites, most often gastrointestinal and skin. Although ovarian disease is seen often as a part of systemic disease, <1% of malignant lymphomas present as an ovarian mass at diagnosis.² Primary ovarian NHL contributes to 0.5% of all NHLs and 1.5% of all malignant ovarian neoplasms³ which makes it an extremely rare entity. Few relevant cases which are published in the literature are included (table 1). Ovarian lymphomas are often diagnosed after surgical removal of ovaries for an ovarian mass lesion, since the clinical features often mimic ovarian carcinoma. The distinction between ovarian lymphoma and carcinoma is made postoperatively, when its extent is evaluated.

The classification of primary and secondary ovarian lymphomas is of prognostic significance, with primary ovarian

Table 1 Comparison table showing the characteristics of previously published cases of Diffuse Large B cell Lymphoma of Ovary in the literature.

Author	Patient age	HIV status	CD20	Laterality	Stage	Treatment	Prognosis (months)
Takashi <i>et al</i> 2002	47	Unknown	Positive	Bilateral	IV	R-CHOP	72
Weingertner <i>et al</i> ⁴	36	Negative	Unknown	Left	IV	Surgery with chemotherapy	12
Mine <i>et al</i> 2013	38	Unknown	Positive	Left	Unknown	Surgery with R-CHOP chemotherapy	24
Jian <i>et al</i> 2014	39	Unknown	Unknown	Left	II	Chemotherapy	6
Jian <i>et al</i> 2014	44	Unknown	Unknown	Bilateral	IV	TAH/BSO with chemotherapy	4
Jian <i>et al</i> 2014	73	Unknown	Unknown	Left	I	LSO with chemotherapy	56
Jian <i>et al</i> 2014	69	Unknown	Unknown	Right	IV	RSO with chemotherapy	4
Jian <i>et al</i> 2014	74	Unknown	Unknown	Left	II	LSO with chemotherapy	40
Jian <i>et al</i> 2014	41	Unknown	Unknown	Left	II	LSO with chemotherapy	36
Jian <i>et al</i> 2014	41	Unknown	Unknown	Left	II	LSO with chemotherapy	7

R-CHOP, cyclophosphamide, doxorubicin, vincristine, prednisolone chemotherapy with the drug rituximab. TAH, Total Abdominal Hysterectomy, BSO, Bilateral Salpingo-oophorectomy, RSO, Right Salpingo-oophorectomy, LSO, Left Salpingo-oophorectomy.

lymphomas having good prognosis with a reported disease-free survival of more than 11 years.⁴

In 1976, Fox *et al*⁵ proposed the criteria for diagnosis of primary ovarian lymphoma:

1. At the time of diagnosis, the lymphoma is clinically confined to the ovary and full investigation fails to reveal evidence of lymphoma elsewhere. A lymphoma can still, however, be considered as primary if the spread has occurred to the immediately adjacent lymph nodes or if there has been a direct 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 ovarian and extraovarian lesions.

Ferrozzi *et al*⁶ reported the typical imaging characteristics of ovarian lymphomas. They were described as a >5 cm frequently bilateral homogeneous mass on ultrasound, CT and MRI. However, in our patient, the CT scan showed a bilateral large heterogeneous adnexal mass, findings consistent with ovarian carcinoma.

It is reported in the literature that unilateral ovarian involvement and focal involvement of the ovary may be indicators of good prognosis, while poor prognostic signs include rapid growth of pelvic mass, severe systemic symptoms, bilateral ovarian tumours and advanced stage at presentation.^{5 7} Note that our patient has primary bilateral ovarian lymphoma, involving the ovaries and regional lymph nodes without any evidence of disease at the remote sites. Also, she remained in remission at 18 months after chemotherapy completion.

Patients diagnosed with DLBCL have a 5% risk of central nervous system (CNS) relapse or progression.⁸ The patients who are at high risk of developing CNS relapse include those with elevated lactate dehydrogenase level, involvement of multiple extranodal sites (eg, bone, kidney, breast, testicle, orbital, epidural spaces and paranasal sinus),^{9 10} high (4–6 factors) International Prognostic Index (IPI) score and with MYC gene rearrangements. Early identification of these patients and giving chemoprophylaxis to prevent CNS relapse is essential. The choice of chemoprophylaxis may include systemic high-dose methotrexate or intrathecal methotrexate. Rituximab also has been shown to reduce the rate of CNS relapse in certain studies.¹¹ Our patient has a good IPI score of 2 without multiple extranodal sites involvement, and no cytological findings on CSF analysis, so CNS prophylaxis was not administered in our case.

The fact that it is a primary bilateral ovarian DLBCL with plasmablastic features and immunostaining negative for CD20 with an imaging pattern suggestive of ovarian carcinoma in an HIV-negative woman makes it an interesting case.

Learning points

- Advanced primary ovarian lymphoma should also be treated with curative intent with combination chemotherapy regimens and surgery based on their specific histology as it is associated with favourable prognosis.
- A CD20-negative plasmablastic variant of diffuse large B-cell lymphoma (DLBCL) has been described as a rapidly progressive tumour, almost exclusively involving the jaw and oral mucosa. It also involves the ovary as described in this case.
- DLBCL is most commonly associated with immunocompromised patients, but it also occurs in immunocompetent patients as described in this case.

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