Received: 16 January 2021 | Revised: 21 October 2021 | Accepted: 26 October 2021

DOI: 10.1002/ccr3.5058

Clinical Case Reports Open Access WILEY

CASE REPORT

Primary bilateral ovarian involvement in Burkitt's lymphoma with an adnexal Torsion-like manifestation: A case report

Mehdi Pourghasemian[1] | **Amin Danandeh Mehr**[1] | **Elaheh Alavizadeh**[1] | **Farhad Behzadi**[2] | **Yousef Roosta**[2,3,4]

[1]Department of Internal Medicine, School of Medicine and Allied Medical Science, Imam Khomeini Hospital, Ardabil University of Medical Sciences, Ardabil, Iran

[2]Department of Internal Medicine, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

[3]Solid Tumor Research Center, Urmia University of Medical Sciences, Urmia, Iran

[4]Hematology, Immune Cell Therapy, and Stem Cells Transplantation Research Center, Clinical Research Institute, Urmia University of Medical Sciences, Urmia, Iran

Correspondence
Yousef Roosta, Department of Internal Medicine, Imam Khomeini Hospital, Urmia University of Medical Sciences, Urmia 5715781351, Iran.
Email: yroosta@gmail.com

Abstract

Burkitt's lymphoma (BL) is defined as a highly invasive B-cell lymphoma with a poor prognosis. Primary bilateral ovarian mass without involvement of other organs is a rare manifestation of BL. Our report was a case of an EBV positive Burkitt's lymphoma, which initially presented with ovarian mass and adnexal torsion.

KEYWORDS

adnexal torsion, Burkitt's lymphoma, EBV infection, primary ovarian lymphoma

1 | INTRODUCTION

Burkitt's lymphoma (BL), a subset of non-Hodgkin's B-cell lymphoma, is an invasive condition with a poor prognosis. In the sporadic form, severe abdominal pain, and rapidly growing abdominal mass are commonly reported, while ovarian involvement is considered a rare manifestation of BL. Here, we represented an EBV-positive primary bilateral ovarian BL in a 14-year-old girl who attended the hospital with a chief complaint of severe abdominal pain. A complete torsion of the right ovary was observed following the ultrasound examination as a primary diagnosis. Next, the result of the immunoglobulin (Ig) test revealed a recent EBV infection (IgG-positive and IgM-negative) in this patient, as well. Finally, the diagnosis of bilateral ovaries BL was established after histopathological and immunohistochemistry examinations and the tumor markers assessment. Eventually, this patient completely recovered following eight cycles of chemotherapy. Although BL is highly progressive, it could be well-controlled with maintaining the quality of life and increasing the patient survival rate upon the early diagnosis.

Burkitt's lymphoma (BL), an aggressive non-Hodgkin's lymphoma (NHL), is mainly associated with B-cell

involvement.[1] According to epidemiological reports, primary ovarian BL accounts for 0.5% of NHL and 1.5% of ovarian cancers.[2] Overall, there are three subtypes of BL, including (1) Endemic BL (classic form), which the patients most likely are associated with Epstein-Barr virus (EBV) infection and can be found in only 20–30% of childhood lymphomas in Africa and the United States.[3–5] The related symptoms encompass an enlargement of the lymph nodes with swelling and distortion of facial bones such as jaw bone and the extra lymph nodes involvement. For the first time, the classic form of the bilateral ovarian lymphoma was reported in a 15-year-old Guantanamo female who referred with fever and abdominal distention, in 1986,[6] (2) sporadic form, in that the prevalence predominantly occurs in western countries such as the UK and among non-African people with ileocecal involvement, abdominal swelling, night sweats, intestinal obstruction, enlarged thyroid or tonsils, and distortion of facial bones, and (3) immunodeficiency-associated BL, which most likely occurs in immunocompromised and HIV-positive people. The symptoms of this subtype are similar to those of the sporadic form..[1,7] EBV, a more common infectious disease among children, is a tumorigenic virus associated with lymphoid tissue disorders such as nasopharyngeal cancer, BL, post-transplant lymphoid disease, B cell, and Hodgkin's lymphoma.[8] However, in non-endemic areas, 80% of BL tumors are not associated with EBV.[9,10] Notably, it has been documented that the pathogenesis of the BL is attributed to the overexpression of c-Myc oncogenes.[11] In ovarian BL, due to the absence of the diffuse symptoms, the "primary" term is used to reflect the origin of the BL from the ovarian lymphatic tissue. It is worth noting that bilateral ovarian resection, one of the therapeutic approaches in young subjects, seems less necessary due to its limited benefits. Hence, following the confirmed diagnosis, intensive chemotherapy should be started as a choice treatment.[12] Although the ovarian BL is one of the fast-growing human tumors and has the potential for doubling during 24–48 h,[13] the intensive chemotherapy in children is more effective than adults, which predominately decreases with age; however, it can affect the patient's fertility as an undesirable effect. Of note, the survival rate of pediatric BL patients is approximately estimated 80%, and invasive chemotherapy in younger patients with BL has a better outcome. Here, the ovarian BL defined by Ann Arbor and St. Jude / Murphy is described in four stages:

Stage I: Solitary tumor as a nodule with a distinct anatomical position in the extrauterine tissues.

Stage II: Single extrauterine tumor or the presence of double extrauterine tumor on one side of the diaphragm.

Stage III: Two extrauterine tumors, paraspinal or epidural mass in the abdomen, two or more nodal areas on opposite sides of the diaphragm.

Stage IV: The advanced stage with the CNS or bone marrow involvement.

According to this classification, our patient was in stage II. There is mounting evidence regarding the sporadic BL occurrence in low-income and developing countries; however, limited reports of this rarely occurred condition have been found in Iran. Given the importance of this issue, we intended to report a new case of the primary bilateral ovarian BL with adnexal torsion manifestation in a young female.

2 | CASE PRESENTATION

A 14-year-old girl was referred to the emergency ward with a chief complaint of severe abdominal pain in the right lower quadrant region without medical history. After admission, a complete blood count (CBC) test was performed to monitor the hemodynamic profile, which showed all parameters in the reference range (Table 1). The serum level of lactate dehydrogenase (LDH) was higher than the reference value (614 U/mL), while the results of liver and kidney function tests seemed normal and beta-human chorionic gonadotropin (β-HCG) was negative. Tumor markers such as CEA, CA-125, CA15-3, and CA19-9 were also measured within the normal range and did not aid in diagnosis. For an early-stage diagnosis, ultrasonography imaging and computed tomography (CT) scan were used. The results showed a complete torsion of the right ovary and the presence of a solid mass (hypoechoic lobular mass) with the size of 136 × 87 mm (Figure 1A,B).

In addition, a bilateral mass on the right ovary (with size 12 × 10 cm) and another mass on the left ovary (with size 13.7 × 13.6 cm) mass were detected during the laparotomy procedure. The right ovarian mass was resected and transferred to the pathology laboratory for further investigation. Postoperatively, the pathological examination verified the peripheral/mature B-cell neoplasm (small non-cleaved cell lymphoma). To identify the involved specific molecular biomarkers, immunohistochemistry (IHC) staining was also performed. Ki-67, a nuclear antigen playing a crucial role in cellular proliferation, is considered a prognostic indicator for cancerous cells detection and is widely used to determine the proliferation rate of the tumor cells.[14] In this case, we also measured the expression of Ki-67 in tumor cells using laboratory-specific Ki-67 staining. As shown in Figure 2A, the amount of Ki-67-positive cells were more than 90% (Figure 2A). Moreover, based on the IHC examination, it has been clarified that among the cluster of differentiation (CD) markers, CD5, CD99, CD3, CD30, OCT4, BCL-2, and WT1 were negative while CD20, as a specific B-cell

TABLE 1 The results of blood laboratory test findings

Hematology				
CBC tests	**Result**	**Unit**	**Reference value**	
W.B.C	9500	Cu/mm	4,000–11,400	
R.B.C	**4.04 L**	Mill.mm^2	M:4.5–6.3 F:4.2–5.4	**Diff** Poly: 61
HB	12.1	Gm/dl	M:14–18; F:12–16	Mono: 3 Lymph: 34 Eos 2
Hct	34.6	%	M; 39–52	
M.C.V	86	Fl	80–96	
M.C.H	**35**	pg	26–32	
M.C.H.C	35	%	32–36	
Platelet	313000	Cu/mm	150,000–450,000	
Biochemistry				
Test	**Result**	**Unit**	**Reference value**	
Urea	23		15–45	
Creatinine	**0.5 L**	Mg/dL	0.6–1.3	
SGOT (AST)	27	IU/L	Up to 31	
SGOT (ALT)	20	IU/L	Up to 31	
ALK. P	100	IU/L	80–1200	
LDH-P	**614**	U/mL	225–500	
Hormonal				
	Result	**Unit**	**Reference value**	
β HCG	<2	Micro IU/mL	1–6 days: 2.5–18 1–20 weeks: 1.7–9.1 Children: 0.7–6.4 Adults: 0.3–5.6 >50 years: Up to 10	

Note: For laboratory values out of reference range, numerical bolding is enough to show significance.

antigen, was positive (Figure 2B). To further substantiate, the c-Myc (8q24) oncogene test was also performed using fluorescence in situ hybridization (FISH) analysis. The result showed that the mutation in 95% of B cells indicated that the c-Myc gene region rearrangement was characterized by two green lights (Figure 2C). Following the karyotype test, a chromosome analysis, the result showed a mosaic karyotype presented by the monosomy on chromosome 10 (Figure 2D). The immune-phenotypic criteria also conformed to our findings. The patient received intravenous chemotherapy with a hyper CVAD regimen, including cyclophosphamide, vincristine, doxorubicin (Adriamycin), and dexamethasone, which was accompanied with methotrexate plus cytarabine (cytosar) treatment for intrathecal (IT) CNS prophylaxis in each cycle. The patient received eight courses of chemotherapy totally, and a complete therapeutic response was obtained. After the treatment, a significant reduction of 90% in the tumor mass dimensions was observed during CT scan imaging (Figure 1C). Since 6 months after the end of the chemotherapy, the disease has not recurred, and she is in a stable situation at present.

3 | DISCUSSION

Burkitt's lymphoma is defined as an NHL, in which tumor cells mainly target the humeral immune system cells called B lymphocytes.[15] The current case report presented a rare sporadic subtype of BL originating from the ovarian tissue with an adnexal torsion-like symptom. Ovarian lymphoma can appear as a primary lesion developing to the aggressive and metastatic form. The sporadic form is commonly observed in patients younger than 35 years

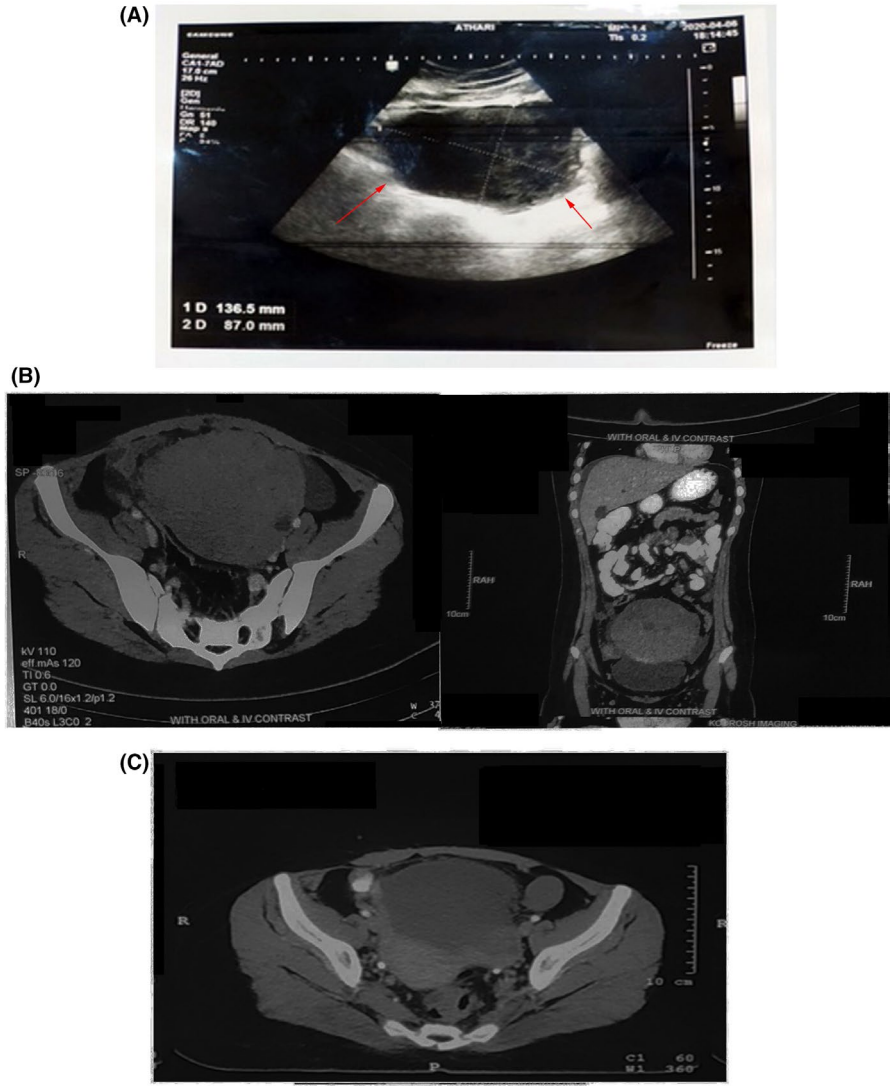

FIGURE 1 (A) Diagnostic imaging with the computerized tomography (CT). CT scan with contrast revealed a large bilateral lobulated adnexal mass. A 136 × 87 mm lobular hypoechoic mass was observed in the right side of the pelvic cavity originated from the right ovary. (B) CT scan of the patient before the onset of the chemotherapy, which indicates a mass on the left side. (C) CT scan represents a significant improvement of the patient after four-cycle chemotherapy

old, and higher incidence among the Caucasus and central American people with the symptom of a large mass in their abdomen.[16] Notably, it has been documented that EBV infects 15% of individuals with sporadic forms.

Moreover, the serum levels of LDH and cancer antigen 125 (CA-125) remarkably increase in patients with BL. In this respect, the serum levels of LDH could be measured from moderate (2000 IU/mL) to high (14,500 IU/mL) levels. Although the serum levels of carbohydrate antigen 19-9 (CA19-9), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), and β-HCG biomarkers usually remain normal in patients with ovarian BL, it can be helpful for the differential diagnosis of other ovarian tumors. Additionally, the evaluation of cerebrospinal fluid (CSF) and bone marrow aspiration for the patients undergoing emission tomography is needed to confirm the diagnosis.[12] In this patient, the levels of CBC and β-HCG were normal; however, the amount of immunoglobulin G (IgG) and IgM was reported positive and negative, respectively, indicating the patient's previous exposure to EBV.

In histopathological examination, the medium-sized monomorphic cells with abundant round nuclei were observed. Due to a large number of macrophages and the monotonous infiltration of lymphocytes, a "starry sky" pattern was also detectable, reflecting the phagocytic clearance of the apoptotic cells.[4] As BL characteristics, the rate of Ki-67-positive cells is most likely close to 100%, and the prognostic biomarkers including BCL-6, CD20, CD22, CD19, CD79a, and CD10 are positively expressed, while CD23, BCL-2, CD5, and terminal deoxynucleotidyl transferase (TdT) were reported negative.[1] In our study, Ki-67 and CD20 positive cells were also observed.

In line with our report, a bilateral ovarian BL in a 31-year-old woman with the chief complaints of general weakness, dyspnea, hyporexia, fever, diaphoresis, weight loss, and abdominal pain was also diagnosed. IHC examination showed positive CD10 and CD20 markers, while tumor cells were negative for CD3 and high Ki-67 proliferative index.[17] Regarding the karyotype test, (8; 14), (2; 8), and (8; 22) chromosomes translocation were identified,

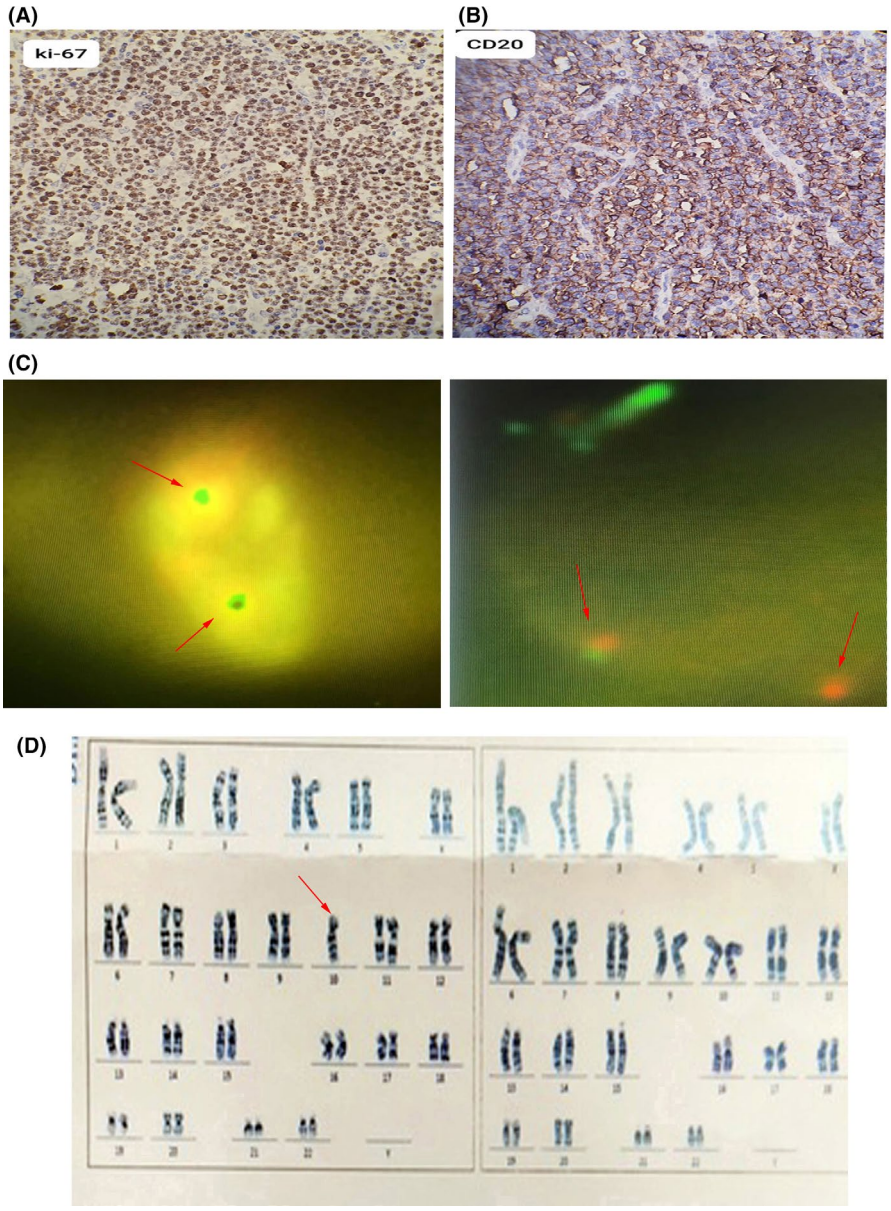

FIGURE 2 (A) The microscopic view of the specific nuclear staining for Ki-67 detection (×100). Ki-67 proliferative index is more than 90% in the tumor cells. (B) CD20-positive diffuse B-cell lymphoma (×100). (C) For assessment of rearrangement in the c-Myc gene, the FISH analysis was used. Green dots show the promotion of 8q24 region rearrangement in 95% of the cells in the left image. Composed red and green dots represent the 8q24 locus rearrangement and establish the mutation of the c-Myc oncogene in the right image. (D) The result of karyotype test demonstrated a chromosome 10 monosomy

mainly related to the c-Myc oncogene.[3] However, we could not find these translocations; instead, a monsoonal chromosome 10 and the c-Myc rearrangement at the 8q24 region were detected, which was a rare but expectable phenomenon.[12] The diagnosis of the disease in the early stages is thought to be very critical, particularly for the specialists to better management of the disease.[12] In detail, stages I and II of the BL are less invasive with limited cell migration and metastatic potential. In contrast, stages III and IV are considered as the advanced phases with a worse prognosis.[5] However, most of the primary ovarian-related malignancies have been diagnosed in the advanced stages. In the present case report, the patient successfully received a CVAD regimen and partially recovered following eight cycles of chemotherapy.

Similarly, a 6-year-old child received four cycles of CODOX-M regimen containing cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate/ifosfamide, etoposide, and high-dose cytarabine following the diagnosis.[18] However, both of the patients recovered after receiving proper treatments. Another study also reported that a 17-year-old girl was admitted to the hospital with severe abdomen pain, palpable pelvic mass, and elevated serum levels of CA-125 2 weeks after the cesarean section. However, this patient expired 19 days after the surgery, without receiving an appropriate chemotherapy regimen.[19]

4 | CONCLUSION

Given that the BL is defined as an invasive malignancy with a high mortality rate worldwide, it could be considered a differential diagnosis of solid ovarian tumors in women, particularly those of reproductive ages.

ACKNOWLEDGEMENTS

We appreciate the patient for her kindly contribution to this study and Dr. Vahedi for precisely performing the c-Myc-specific staining.

CONFLICT OF INTEREST

The authors indicated that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

MP participated in the pathological results interpretation and disease diagnosis; AD edited the manuscript and finalized it; EA prepared the first draft; FB collected the data; and YR conceived the project.

CONSENT

The informed consent was obtained from the patient, who willingly participated in this report.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Mehdi Pourghasemian https://orcid.org/0000-0002-1540-1400
Amin Danandeh Mehr https://orcid.org/0000-0002-9063-8539
Elaheh Alavizadeh https://orcid.org/0000-0003-0654-3973
Yousef Roosta https://orcid.org/0000-0003-4144-6482

REFERENCES

1. Chabner BA. *Harrison's manual of oncology*. McGraw-Hill; 2008.
2. Crasta JA, Vallikad E. Ovarian lymphoma. *Indian J Med Paediatr Oncol*. 2009;30(1):28.
3. Haluska FG, Tsujimoto Y, Croce CM. The t (8; 14) chromosome translocation of the Burkitt lymphoma cell line Daudi occurred during immunoglobulin gene rearrangement and involved the heavy chain diversity region. *Proc Natl Acad Sci*. 1987;84(19):6835-6839.
4. Brady G, MacArthur G, Farrell P. Epstein-Barr virus and Burkitt lymphoma. *Postgrad Med J*. 2008;84(993):372-377.
5. Huang H, Liu Z-L, Zeng H, et al. Clinicopathological study of sporadic Burkitt lymphoma in children. *Chin Med J*. 2015;128(4):510.
6. Weekes LR. Burkitt's lymphoma of the ovaries. *J Natl Med Assoc*. 1986;78(7):609.
7. Govindan R, DeVita VT. *DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology Review*. Lippincott Williams & Wilkins; 2009.
8. Sar N. Detection of Epstein-Barr virus infection in lymphoma: ELISA and PCR method. *Tehran Univ Med J TUMS Publications*. 2010;67(11):787-792.
9. Hoda SA, Cheng E. *Robbins basic pathology*. Oxford University Press US; 2017.
10. Montes-Moreno S, Odqvist L, Diaz-Perez JA, et al. EBV-positive diffuse large B-cell lymphoma of the elderly is an aggressive post-germinal center B-cell neoplasm characterized by prominent nuclear factor-kB activation. *Mod Pathol*. 2012;25(7):968-982.
11. Norris D, Stone J. *WHO classification of tumours of haematopoietic and lymphoid tissues*. WHO; 2008:22-23.
12. Stepniak A, Czuczwar P, Szkodziak P, Wozniakowska E, Wozniak S, Paszkowski T. Primary ovarian Burkitt's lymphoma: a rare oncological problem in gynaecology: a review of literature. *Arch Gynecol Obstet*. 2017;296(4):653-660.
13. Molyneux EM, Rochford R, Griffin B, et al. Burkitt's lymphoma. *Lancet*. 2012;379(9822):1234-1244.
14. Li LT, Jiang G, Chen Q, Zheng JN. Ki67 is a promising molecular target in the diagnosis of cancer. *Mol Med Rep*. 2015;11(3):1566-1572.
15. Schmitz R, Young RM, Ceribelli M, et al. Burkitt lymphoma pathogenesis and therapeutic targets from structural and functional genomics. *Nature*. 2012;490(7418):116-120.
16. Dozzo M, Carobolante F, Donisi PM, et al. Burkitt lymphoma in adolescents and young adults: management challenges. *Adolesc Health Med Ther*. 2017;8:11.
17. Briseño-Hernández AA, Quezada-López DR, Castañeda-Chávez A, Macías-Amezcua MD, Pintor-Belmontes JC. Bilateral ovarian Burkitt's lymphoma. A case presentation. *Cirugia y Cirujanos*. 2014;82(2):212-218.
18. Mondal SK, Bera H, Mondal S, Samanta TK. Primary bilateral ovarian Burkitt's lymphoma in a six-year-old child: report of a rare malignancy. *J Cancer Res Ther*. 2014;10(3):755-757.https://doi.org/10.4103/0973-1482.136026
19. Wamalwa EW, Chumba DK, Keitany KK, Patel K. Bilateral primary ovarian Burkitt's lymphoma. *Indian J Gynecol Oncol*. 2018;16(1):8. https://doi.org/10.1007/s40944-018-0178-9

How to cite this article: Pourghasemian M, Danandeh Mehr A, Alavizadeh E, Behzadi F, Roosta Y. Primary bilateral ovarian involvement in Burkitt's lymphoma with an adnexal Torsion-like manifestation: A case report. *Clin Case Rep*. 2021;9:e05058. https://doi.org/10.1002/ccr3.5058