VIA MEDICA

CASE REPORT

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A case of B-cell lymphoma of the uterus

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ABSTRACT

Primary malignant lymphoma occurs rarely in the female reproductive tract. A case of a 64-year-old female patient diagnosed with B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma (B-UCL) of the uterus is presented. The patient underwent three cycles of chemotherapy based on R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone combined with rituximab), radiation therapy to the pelvis, and extended hysterectomy. The follow-up has been conducted for three years. No sign of disease recurrence has been observed in physical examination and on images.

Key words: uterus, B-cell lymphoma, Burkitt lymphoma, unclassifiable B-cell lymphoma, primary malignant lymphoma

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Introduction

Common extranodal malignant lymphomas are located mainly in the gastrointestinal tract and skin [1]. However, as little as 0.5% of the lymphomas may occur in the uterus, and the most common type is diffuse large B-cell lymphoma [1–3]. The most frequently observed symptoms of the lymphoma of the uterus are: abnormal vaginal bleeding and abdominal pain [4]. Specific treatment of uterine lymphomas has not been established [4]. In this article a B-UCL case growing in the uterine corpus is discussed. To date, no case of B-UCL in the gynaecological tract has been reported.

Case presentation

A 64-year-old patient with a history of hypertension, diabetes, asthma, and strumectomy presented with abnormal vaginal blood loss and dizziness for the preceding three months. No previous gynaecological disorders were noted. The patient had six children and one history of miscarriage. An endometrial scraping was performed, and histopathological examination revealed the presence of primary malignant lymphoma. Contrast computed tomography (CT) showed an enlarged uterus measuring approximately 13 × 7 cm without any evident lesions, slightly heterogenous within the fundus. No regional and distant enlarged lymph nodes were revealed (Fig. 1A and B). An endometrial scraping was repeated. Histopathological examination revealed B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma. CD20 positivity in 95% of the cells, Ki67 in 85% of the cells, and focal expression of vimentin and CD3 were observed. Laboratory data showed elevated LDH levels. Full blood count was normal. She did not have a history suggestive bleeding disorder. A cerebrospinal fluid examination demonstrated no abnormal cells. 18F-fluoro-2-deoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) showed increased glucose metabolism exclusively in the uterine. The clinical stage of the disease was IA and international prognostic index 2 (IPI-2), thus systemic therapy based on rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) every 21 days was initiated. Despite the fact that prophylaxis with pegfilgrastim was implemented, after the third course of chemotherapy the patient experienced febrile neutropaenia, severe dyspnoea, pneumonia, and deterioration of general status

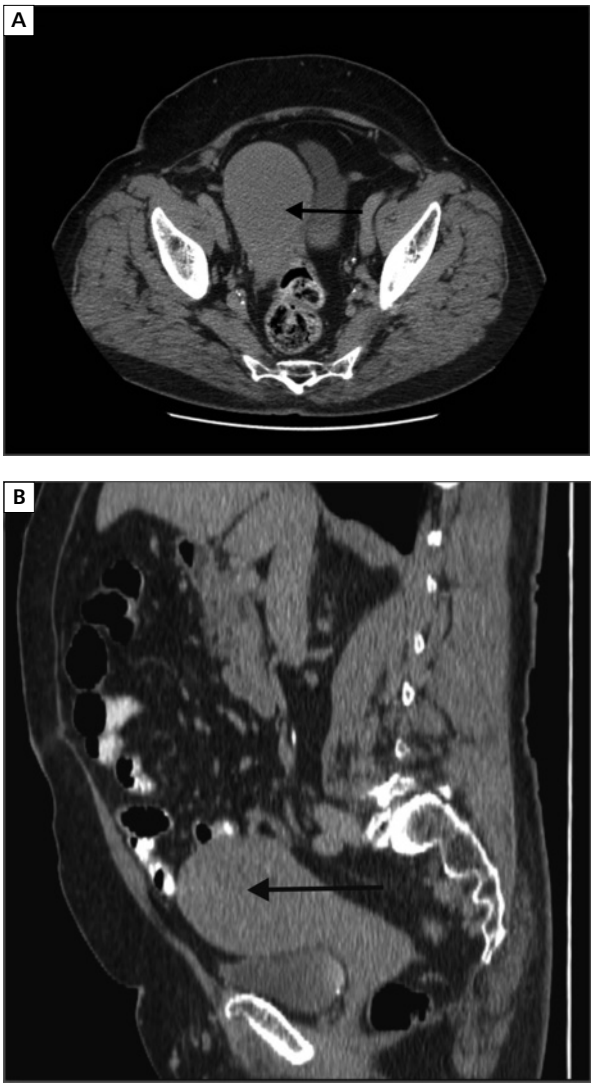

Figure 1. Computed tomography of the pelvic area showing enlarged uterus (arrows) diagnosed as B-cell lymphoma

performance. R-CHOP treatment was discontinued. An abdominal/pelvic CT examination after the third cycle of chemotherapy showed partial regression of the malignancy. Thereafter, the patient underwent radical photon megavoltage 3D intensively modulated radiation therapy (IMRT) to the uterus at the dose 40 Gy delivered in 20 fractions. Two months after the radiotherapy cessation the patient developed sigmoid abscess, which was treated with antibiotics. The CT exam revealed slightly larger uterus in comparison to pre-radiotherapy size but much slower than at diagnosis. The gynaecological ultrasonography revealed presence of fluid width 3.5 mm, and a hypoechoic area measuring 21.3 × 13.9 mm in the uterus' posterior wall. Two months later the patient developed abdominal pain. Extended hysterectomy was performed. Postoperative histopathological examination demonstrated no microscopic disease in the atrophic endometrium. The patient has been free from lymphoma for three years.

Discussion

Primary lymphomas of the uterus are rare extranodal lymphomas (ENLs) with non-specific symptoms that may delay diagnosis [1]. The most common type of uterus lymphoma is diffuse large B-cell lymphoma (DLBCL). Low-stage masses commonly occur in the uterine cervix, whereas high-stage cases include the cervix or the corpus of the uterus [1, 4]. Genital lymphomas often stay unnoticed during ultrasound, CT, or MRI examination, which is why FDG-PET/CT has become an important method of diagnosing patients with lymphomas [2]. The presented patient complained of abnormal bleeding and abdominal pain. CT scans showed enlarged uterus with heterogeneous fundus, without any evident lesions, while the FDG-PET/CT examination revealed a mass with increased glucose metabolism. The patient was finally diagnosed with B-UCL. No data of B-UCL presence in the female genital tract have been found in the literature. What is important, the 2016 revision of the World Health Organisation classification of lymphoid neoplasms introduced some changes in the nomenclature of lymphomas [5]. High-grade B-cell lymphoma, NOS, together with the new category for the "double-/ /triple-hit" lymphomas, replaces the 2008 category of B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and Burkitt lymphoma (BCLU). It includes now blastoid-appearing large B-cell lymphomas and cases lacking MYC and BCL2 or BCL6 translocations that would formerly have been called BCLU.

Different managements of the uterus lymphoma were reported in the literature: chemotherapy, radiotherapy, hysterectomy alone or in the combination [3, 6–8]. Different chemotherapy regimens have been used: MACOP-B (methotrexate, cytarabine, cyclophosphamide, vincristine, prednisolone, bleomycin), CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone), CVP (cyclophosphamide, vincristine, prednisolone), CHOP-bleo (cyclophosphamide, doxorubicin, vincristine, prednisolone, bleomycin), ASAP (doxorubicin, methylprednisolone, cytarabine, cisplatin), CEOP (cyclophosphamide, etoposide, vincristine, prednisolone), BACOD (bleomycin, doxorubicin, cyclophosphamide, vincristine), and R-CHOP [9]. Unfortunately, only short retrospective studies are available in the literature-presented patients with aggressive B-cell lymphomas of different location [10–13] and even less is devoted to the location of the lymphoma in gynaecological tract [6–8]. The study carried out in the Department of Pathology and Microbiology in Nebraska Medical Centre

gave the result that most of the patients diagnosed with the B-UCL were older, with an average age of 69 years [10]. The majority of patients presented advanced-stage disease and high IPI scores (3–5), with median of overall survival of nine months and five-year overall survival of 30%. Patients with lower IPI scores (0–2) had slightly better prognosis [10]. Furthermore, the study revealed no predictive features of survival in immunochemistry or genetics. Both groups of patients demonstrated poor response to the therapy [10]. Similarly, analysis from Argentina showed the mean age of BCLU patients as 70 years and significantly shorter survival time of BCLU patients (mean 6.6 months) in comparison to DLBCL (31 months) and BL (30 months), respectively [12]. The BCLU patients three-year overall survival (OS) was 62% and the three-year event-free survival (EFS) was 51% in a Russian study [13]. The prognosis of BCLU patients depended on the presence of BCL2 and MYC expression (double-hit lymphoma, DHL group). However, the three-year OS was lower for the DHL group than that for the non-DHL group (43 and 75%, respectively).

Although there is no specified treatment method of the B-UCL/High-grade B-cell lymphoma, NOS localised in the uterus it seems that International Lymphoma Radiation Oncology Group recommendations for extranodal lymphomas should be applied in such cases [14]. According to guidelines, the aggressive lymphomas in early stages (I, II) may be treated by chemotherapy alone (approx. six courses) or radiochemotherapy (approx. three courses). In the latter approach short regimens of chemo- or immunochemotherapy should be followed by involved site radiochemotherapy — ISRT. The field should cover the whole organ with a 1-cm margin of surrounding tissues. The dose ranges between 30 and 40 Gy depending on metabolic response after chemotherapy. Our patient's response to R-CHOP was positive and partial response in the uterus was achieved. However, because the tolerance of the systemic treatment was poor (the patient developed febrile neutropaenia) the radiation was initiated after three courses of immunochemotherapy. Hysterectomy performed a few months later confirmed complete response after irradiation. Since no evidence-based treatment recommendations exist in the rare case of B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma (B-UCL)/ /high-grade B-cell lymphoma, NOS, multidisciplinary decisions have to be made to individualise the treatment option for each patient.

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