Clinical Case Report

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Successful conservative treatment of primary endometrial marginal zone lymphoma (MALT type)

A case report and review of the literature

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Abstract

Rationale: Primary endometrial marginal zone lymphoma (mucosa-associated lymphoid tissue [MALT] type) is a rare histological type of non-Hodgkin lymphoma (NHL); therefore, this disease is challenging to diagnosis and treatment.

Patient concerns: A 61-year-old (gravidity 2, parity 2) female was admitted complaining of postmenopausal vaginal bleeding for 2 months.

Diagnoses: An ultrasound revealed a slightly thickened endometrium. Histology revealed a dense lymphoid infiltrate in the endometrium, which was suggestive of an NHL. The atypical lymphocytes were positive for CD20 and BCL-2. Moreover, the PCR demonstrated monoclonal heavy chain gene rearrangement. Taken together, the diagnosis of primary endometrial marginal zone lymphoma (MALT type) was established. According to Ann Arbor criteria, the disease was staged IEA.

Interventions: Dilatation and curettage was performed, and no additional surgery or radiotherapy and chemotherapy was administered.

Outcomes: The patient was alive with no evidence of cancer for ≥41 months.

Lessons: Primary endometrial marginal zone lymphoma (MALT Type) is a very rare indolent tumor, and its prognosis seems to be good. Thus, conservative treatment and no further therapy were suggested based on the tumor biology.

Abbreviations: CT = computed tomography, D&C = dilatation and curettage, EMZL = extranodal marginal zone lymphoma, IHC = immunohistochemistry, MALT = mucosa-associated lymphoid tissue, NHL = non-Hodgkin lymphoma.

Keywords: conservative treatment, endometrium, marginal zone lymphoma, non-Hodgkin lymphomas

1. Introduction

Primary uterine lymphoma accounts for <1% of extranodal lymphomas, most of which arise in the cervix.[1] Primary endometrial lymphomas are exceptionally rare. To our knowledge, 20 cases of primary endometrial marginal zone lymphoma (mucosa-associated lymphoid tissue [MALT] type) have been reported in the English-language literature.[2–10] The lack of information on the morphologic spectrum, together with the relatively brief follow-up of prior cases, has hampered classification of these abnormal lymphoid proliferations into the endometrium. We report herein a case of primary endometrial marginal zone lymphoma (MALT type) that showed a good outcome after conservative treatment.

2. Case presentation

A 61-year-old (gravidity 2, parity 2) female was admitted due to postmenopausal vaginal bleeding. She had no significant medical history and no family history of carcinoma. The findings of a chest X-ray and full blood count were normal, as were those of computed tomography (CT) of the abdomen and pelvis. An ultrasound examination revealed a slightly thickened endometrium. The patient subsequently underwent dilatation and curettage (D&C).

Grossly, the specimen was endometrial tissue of 1.5 × 1.0 × 1.0 cm. Microscopically, the endometrium was infiltrated by a monotonous, dense proliferation of small-to-medium-sized atypical lymphoid cells. In some areas, the lymphocytes had scant cytoplasm and slightly irregular nuclei with inconspicuous nucleoli. Scattered transformed blasts were admixed with the small-cell population, and no sign of plasma-cell differentiation was noted (Fig. 1A–C).

Editor: N/A.

This study was approved by the ethics committee of the Women's Hospital, Zhejiang University School of Medicine (20170171).

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

The datasets during and/or analyzed during the present study available from the corresponding author on reasonable request.

The authors have no funding and conflicts of interests to disclose.

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Medicine (2019) 98:16(e15331)

Received: 16 December 2018 / Received in final form: 19 March 2019 / Accepted: 25 March 2019

http://dx.doi.org/10.1097/MD.0000000000015331

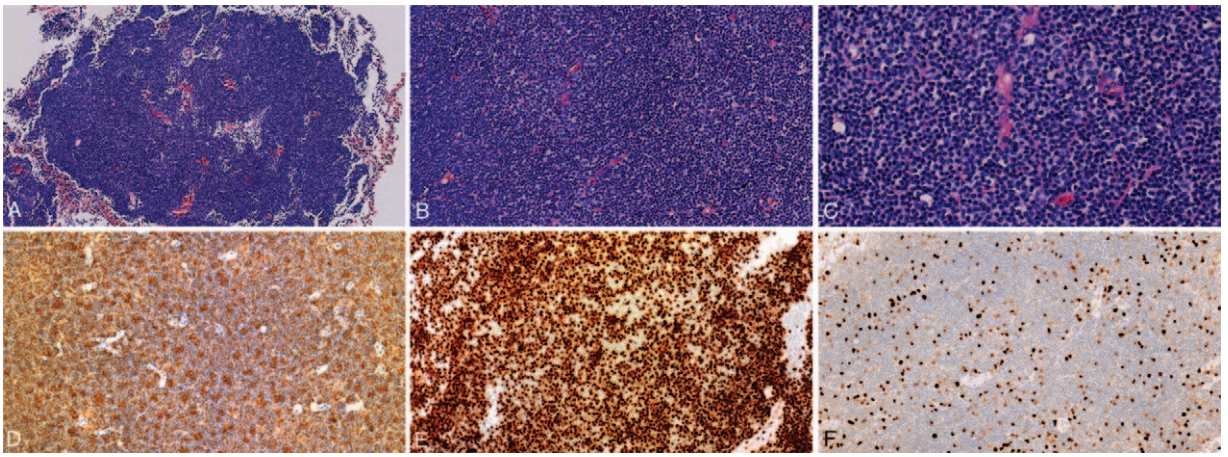

Figure 1. Histology of endometrial tissue shows a dense of small-sized to medium-sized atypical lymphocytes with clear cytoplasm and irregular (A, 10×, B, 20×), slightly indented nuclei (C, 40×). Immunohistochemical stains show CD20 (D, 20×) and BCL-2 (E, 20×) positive lymphocytes. The index of Ki67 (F, 20×) was 15%.

Immunohistochemistry (IHC) showed that the atypical lymphocytes were positive for CD20 (Fig. 1D) and BCL-2 (Fig. 1E) and negative for CD5, CD10, BCL-6, cyclinD1, and CD23. The proliferation index, as assessed by Ki-67 IHC, was 15% (Fig. 1F). B-cell gene-rearrangement analysis was conducted using the IGH&IGK Kit (Rightone Technology, China) and 3500Dx Genetic Analyzer software (Thermo-Fisher, Waltham, MA), according to the manufacturer's protocol. Immunoglobulin heavy-chain locus rearrangements were demonstrated (Fig. 2).

Thus, we established a diagnosis of primary endometrial marginal zone lymphoma (MALT type). Bone marrow biopsy revealed no evidence of lymphoma. According to Ann Arbor

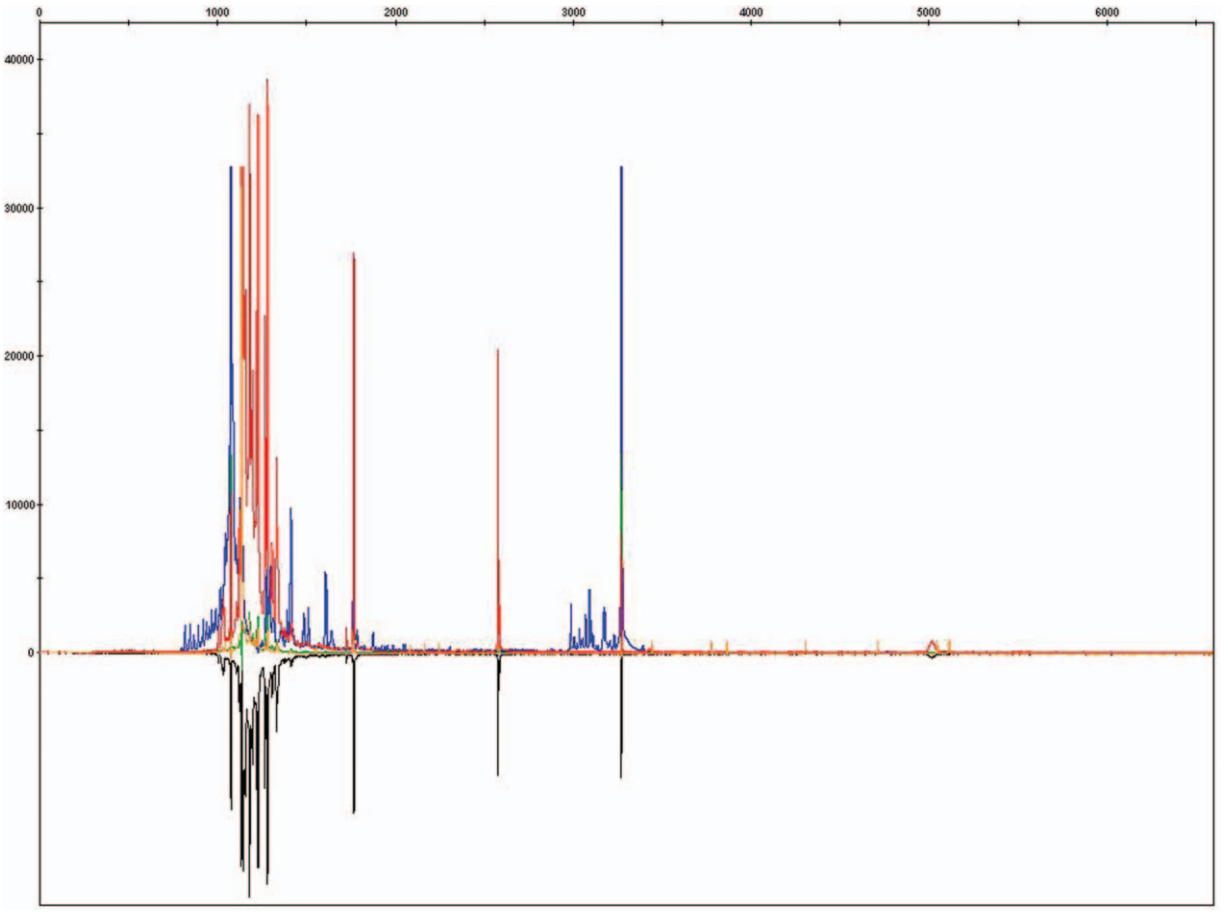

Figure 2. The demonstration of a clonal immunoglobulin heavy-chain locus rearrangement, IGHB.

Table 1

Successful conservative treatment of primary endometrial marginal lymphoma (MALT type) reported in the English medical literature.

Case no. [Ref.]	Age	Clinical presentation	Clinical history	Site	Histologic grade	IgH gene rearrangement	BM involvement	Ann Arbor stage	Treatment	Follow-up
1[2]	81	Endometrial polyp	Breast cancer	EM and polyp	Low	N/A	N	IEA	Polyp excision	ned at 12 mo
2[9]	72	Foul smelling bloody discharge	N	EM	Low	Y	N	IEA	D&C	ned at 60 mo
Pre	61	Postmenopausal vaginal bleeding	N	EM	Low	Y	N	IEA	D&C	ned at 41 mo

BM = bone marrow, D&C = dilatation and curettage, EM = endometrium, IgH = immunoglobulin heavy chain, ned = no evidence of disease, N = no, Pre = present case, Y = yes.

criteria, the disease was staged IEA. Therefore, conservative treatment and no further therapy were recommended based on the tumor biology. At the time of writing, the patient had survived with no evidence of cancer for ≥41 months.

3. Discussion

Primary endometrial marginal zone lymphoma (MALT type) is a rare tumor, few cases of which have been reported.[2–10] Based on prior reports and our case, the most common clinical symptom is postmenopausal or perimenopausal vaginal bleeding/discharge. In the current case, the patient was of typical age and exhibited a typical clinical presentation. The diagnosis was supported by morphologic, IHC, and molecular analyses.

The immunohistochemical profile is useful for diagnosing non-Hodgkin lymphoma (NHL). The most frequently used markers are CD3, CD5, CD10, CD20, CD23, CD43, CD79a, BCL-2, BCL-6, cyclinD1, and ki-67.[1] However, these markers are nonspecific. In our case, IHC suggested an extremely rare malignant B-cell lymphoma of the endometrium. Importantly, the expression of NHL markers should be combined with morphological features. In addition, B-cell gene rearrangements should be investigated.

Most lymphomas in the uterus are secondary to systemic lymphoma, with the cervix being the most frequent site.[1] Primary endometrial marginal zone lymphoma (MALT type) is diagnosed on the basis of the following criteria[11]: at the time of initial diagnosis, the lymphoma was primarily confined to the uterine cavity and extensive work-up did not reveal evidence of lymphoma at any other site; no evidence of leukemic phase; and a fairly long interval between the appearance of primary lymphoma and secondary involvement. The patient described herein met these criteria.

The etiology and pathogenesis of extranodal marginal zone lymphoma (EMZL) are unclear, but are associated with chronic infections and autoimmune diseases. Various microorganisms may cause EMZL at mucosal or cutaneous sites. For example, *Helicobacter pylori*, *Chlamydia psittaci*, *Campylobacter jejuni*, and *Borrelia burgdorferi* are reportedly related to gastric mucosa-associated lymphoid tissue or MALT lymphoma, ocular adnexal EMZL lymphoma, immunoproliferative small-intestinal disease, and cutaneous EMZL, respectively.[12] However, there was no evidence of chronic endometritis in the present case.

Primary endometrial marginal zone lymphoma (MALT type) should be distinguished from benign reactive conditions and small-cell lymphomas. Other small-cell lymphomas such as chronic lymphocytic leukemia/small lymphocytic lymphoma, follicular lymphoma, and mantle cell lymphoma can be ruled out by IHC. Negativity for CD5 and CD23 excludes small-cell lymphocytic lymphoma, and negativity for cyclinD1 rules out mantle-cell lymphoma. The absence of follicular-pattern lymphoid cell infiltration and negativity for BCL-6 and CD10 rule out follicular lymphoma.[7,8]

As a consequence of the low incidence of primary uterine NHL, there is no approved treatment protocol and no clear association between the outcome and treatment modality has been established. Extranodal marginal zone B-cell lymphomas are regarded as indolent tumors; the 5-year cause-specific survival rate is 94%.[13] Patients with primary endometrial marginal zone lymphoma (MALT type) in prior reports had a good prognosis and none died during the follow-up period.[2–10] However, most of the patients underwent total hysterectomy,[4–8,10] and one patient received additional pelvic and paraaortic lymph node radiotherapy.[5] Only 3 patients,[2,9] including ours, were treated with D&C rather than additional surgery or radiotherapy and chemotherapy (Table 1).

4. Conclusion

The prognosis of patients with primary endometrial marginal zone lymphoma is related to the stage, location, and biology of the lymphoma. Our patient presented with no symptoms and her blood sample and bone marrow biopsy revealed no evidence of lymphoma, which is in accordance with the generally indolent character of this condition. Thus, conservative treatment was recommended.

Author contributions

Resources: Xiuming Zhang, Feng Zhou.
Supervision: Feng Zhou.
Writing – original draft: Xiuming Zhang.
Writing – review and editing: Feng Zhou.

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