CASE REPORT

Chronic lymphocytic leukaemia masquerading as a labial lump

Wei How Lim,^{1,2} Eleni Mayson,^{2,3} Vincent P Lamaro^{1,2,4}

¹Department of Gynaecology, St Vincent's Hospital, Darlinghurst, New South Wales, Australia

²UNSW Medicine, St Vincent's Clinical School, Darlinghurst, New South Wales, Australia

³Department of Haematology, The Kinghorn Cancer Centre, Darlinghurst, New South Wales, Australia

⁴Clinic 404, St Vincent's Clinic, Darlinghurst, New South Wales, Australia

Correspondence to

Dr Wei How Lim,
weihowlim@gmail.com

Accepted 12 December 2018

SUMMARY

We report a case of an 82-year-old woman who presented with a 2-week history of a left labial lump. She had a history of chronic lymphocytic leukaemia (CLL) for several years and remained stable without clinical evidence of disease progression. She was observed with regular blood tests and clinical assessment. She was hypogammaglobulinaemic from the CLL and due to frequent symptomatic infections requiring hospitalisation, was commenced on monthly intravenous immunoglobulin. A tissue biopsy of the labial lump confirmed involved CLL in the genital area and further investigations and management followed.

BACKGROUND

Chronic lymphocytic leukaemia (CLL) is a lymphoproliferative condition characterised by the presence of functionally incompetent mature B lymphocytes in the blood, bone marrow and lymphoid tissues, most of which are monoclonal.¹ Although CLL is currently incurable, the clinical course varies significantly, with some patients remaining symptom free and not requiring any treatment for many years. CLL and its lymph-node predominant equivalent

Figure 2 Heavy infiltrate of small lymphocytes showing a sheet-like arrangement. (H&E, $\times 100$).

small lymphocytic lymphoma require observation until there is clinical evidence for treatment, nowadays encompassing more than just a rising lymphocyte count. Indications for treatment include disease progression, cytopenias, autoimmune complications or recurrent infections. Treatment in most cases involves a combination of chemotherapy and immunotherapy.² The extra-nodal manifestation of CLL in the vulvovaginal area is an unusual location for organ involvement, and we described our experience with such a clinical presentation and discussed our assessment and management.

CASE PRESENTATION

An 82-year-old Lithuanian woman presented with a swollen left labial lump for 2 weeks duration. She had a history of CLL (Rai Stage IV/Binet C) which

Figure 1 Left labial lump measuring 5x5 cm encompassing the left minora and majora.

Figure 3 Positive staining of CD23 abnormal B lymphocytes. (Immunohistochemistry, $\times 100$).

© BMJ Publishing Group Limited 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Lim WH, Mayson E, Lamaro VP. *BMJ Case Rep* 2019;**12**:e227328. doi:10.1136/bcr-2018-227328

Figure 4 CT chest, abdomen and pelvis showing 1—an enlarged spleen (17 cm size) and 2—an enlarged left inguinal lymph node (3 cm size).

remained stable and was being monitored by her haematologist with regular blood tests. Her lymphocyte count remained consistently below $50 \times 10^9/L$ and she had a mild compensated anaemia and thrombocytopaenia, both autoimmune complications from the CLL. She was hypogammaglobulinaemic from the CLL, and qualified for monthly IV immunoglobulin. Her other comorbidities included chronic kidney disease, hypertension, depression and atrial fibrillation on apixiban.

On examination, a 5×5 cm non-tender firm left labial lump was noted (figure 1). She had a tippable spleen but no peripheral lymphadenopathy or petechiae. An incision on the lump revealed mainly indurated tissue and a biopsy was performed.

INVESTIGATIONS

The biopsy of the labial lump showed vascular fibroadipose tissue with an infiltrate of small lymphoid cells in a diffuse pattern without normal lymphoid follicle formation (figure 2).

On immunoperoxidase staining, the lymphoid tissue was composed of small lymphocytes with CD5+/CD20+/CD23 +B cells (figure 3). Staining for CD10 and cyclin D1 were negative. No CD21 dendritic networks were seen. The Ki67 proliferation index was approximately 30%. Flow cytometry on the sample was consistent with the immunophenotype of CLL. Overall, the biopsy confirmed labial tissue involvement with CLL, rather than contamination by CLL-lymphocytes, which can sometimes occur.

As part of her work-up, a CT chest/abdomen/pelvis was performed and revealed splenomegaly as well as deep left inguinal lymphadenopathy (figure 4). A Positron Emission Tomography (PET) scan showed increased fluoro-deoxyglucose (FDG) uptake in the left inguinal lymph nodes, with confluent mild to moderate volume nodal disease in the para-aortic region.

No other abnormal hypermetabolism was detected in both lymphatic and extra-lymphatic sites.

A bone marrow aspirate/trephine was performed and revealed 95% infiltration with small mature lymphocytes and markedly reduced erythropoiesis and granulopoiesis. Flow cytometry on the aspirate was consistent with CLL, being positive for CD5, CD19, CD20 (dim), CD22, CD23 and CD200. Bone marrow cytogenetic and fluorescence in situ hybridisation (FISH) studies revealed trisomy 12 only. Importantly, the 17p deletion was not detected. A core biopsy of the left inguinal lymph node confirmed CLL, importantly with no large cell transformation.

DIFFERENTIAL DIAGNOSIS

Labial lump in premenopausal and postmenopausal women may include:

- ▶ Cellulitis.
- ▶ Vulval malignancy.
- ▶ Cyst or abscess collection.
- ▶ Indurated tissue from chronic inflammation.

TREATMENT

Given the unusual extra-nodal presentation of CLL in the labia, treatment was indicated. Combination therapy was chosen given the patient's age and comorbidities incorporating the anti-CD20 antibody obinutuzumab and chemotherapy chlorambucil as the first line of management.

OUTCOME AND FOLLOW-UP

Clinically our patient responded well to six cycles of chemoimmunotherapy, with complete resolution of her labial lump. Radiotherapy may be considered if symptomatic residual disease persists.

DISCUSSION

We present a rare extra-nodal manifestation of CLL with labial infiltration that warranted treatment. Staging investigations including a PET scan and biopsy of an FDG-avid lymph node were essential to exclude a Richter's transformation. Bone marrow biopsy including cytogenetic and FISH studies was necessary to prognosticate the disease, as well as to exclude the 17p deletion—a poor prognostic feature for which treatment with the BTK inhibitor ibrutinib is instead indicated. Given the patient's age and comorbidities, together with the information from her bone marrow cytogenetics, combination chemoimmunotherapy with obinutuzumab/chlorambucil was chosen.

Vaginal 'lumps and bumps' are common clinical presentations for general practitioners and gynaecologists. A tissue biopsy diagnosis should be undertaken for women with recurrent lesions or in the postmenopausal period to exclude malignancy and other unusual pathology that may arise. A background medical history of chronic illnesses is often associated with being immunocompromised, predisposing to opportunistic infection that may result in chronic inflammation and eventual cell atypia. Therefore a tissue biopsy was important in our patient's case and guided the appropriate management.

Obtaining adequate tissue for histopathology and incorporating flow cytometry analysis in the case of our patient with CLL are essential to confirm the diagnosis and exclude contamination of other lymphoid malignancies and Richter's transformation (transformation to a high grade lymphoma) which can occur at a rate of 2%–15% for patients with CLL and would alter treatment and prognosis.³ In addition to an increased risk of infections, patients with CLL (regardless of whether it has been treated) are at increased risk of developing secondary

malignancies, especially cutaneous lesions such as squamous cell carcinoma and melanoma.^{3 4}

Extra-nodal involvement with CLL is previously described, with cutaneous manifestations (leukaemia cutis) being the most common. Such manifestations need to be differentiated from other lesions including secondary cutaneous malignancies. The female reproductive system is a rare and unusual location for such lymphoid disease involvement, and we believe that our patient is the fourth reported in the English literature to date to involve the vulvovagina.^{5–7}

We hope our case study serves as an important clinical reminder to always investigate and obtain an adequate tissue biopsy for

postmenopausal women who presents with a labial or vulval mass. A multidisciplinary team management approach is important to reach a diagnosis and to offer the most appropriate care.

Contributors All three authors were directly involved in the clinical care of the patient illustrated in the manuscript. WHL obtained informed consent from the patient and wrote the manuscript. Both EM and VPL reviewed and edited the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Learning points

- Presentation of a labial/vulval lump in a postmenopausal woman warrants further investigation.
- Adequate tissue biopsy is essential to exclude malignancy and other unusual pathology.
- Clinical evidence of chronic lymphocytic leukaemia (CLL) disease progression may include unusual extranodal involvement.
- When managing patients with CLL, a high index of suspicion for Richter's transformation (transformation to high grade lymphoma) should prompt the clinician to perform adequate biopsies to exclude this diagnosis. The treatment and prognosis of Richter's transformation is different to CLL.

REFERENCES

- 1 Dighiero G, Hamblin TJ. Chronic lymphocytic leukaemia. *Lancet* 2008;371:1017–29.
- 2 Parikh SA, Rabe KG, Call TG, *et al.* Diffuse large B-cell lymphoma (Richter syndrome) in patients with chronic lymphocytic leukaemia (CLL): a cohort study of newly diagnosed patients. *Br J Haematol* 2013;162:774–82.
- 3 Agnew KL, Ruchlemer R, Catovsky D, *et al.* Cutaneous findings in chronic lymphocytic leukaemia. *Br J Dermatol* 2004;150:1129–35.
- 4 Kipps TJ, Stevenson FK, Wu CJ, *et al.* Chronic lymphocytic leukaemia. *Nat Rev Dis Primers* 2017;3:17008.
- 5 Udupa K, Ganesan P, Majhi U, *et al.* Unusual involvement of cervix and vulva in a case of chronic lymphocytic leukemia. *J Gynecol Oncol* 2012;23:205–6.
- 6 Katsnelson M, Laughingwell R, Rose LJ, *et al.* Colposcopic and cytologic detection of chronic lymphocytic leukemia in the vagina: a case report. *J Reprod Med* 2011;56:344–6.
- 7 Mikhail MS, Runowicz CD, Kadish AS, *et al.* Colposcopic and cytologic detection of chronic lymphocytic leukemia. *Gynecol Oncol* 1989;34:106–8.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow