Case Report
Plasmablastic lymphoma involving the breast: report of a case and review of literature

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Abstract: Background: Plasmablastic lymphoma (PBL) is a rare entity of non-Hodgkin lymphomas that usually occurs in the oral cavity in immunocompromised patients. PBL involving the other sites have rarely been reported. Case report: Herein, we report a rare case of EBV-negative PBL in the left breast of an immunocompetent 56-year-old woman. During physical examination, she had left breast masses and left axillary lymphadenopathy. After surgical resection of the neoplasm, histological and cytological examinations were performed and the tumor was diagnosed to be primary PBL. Tumor cells expressed VS38c and some were MUM1-positive, but were negative for common leucocyte antigen CD45, pan-B cell markers CD20 and CD79a, plasma cell marker CD138, EMA, CD38, CD56, PAX5, ALK. Ki-67 immunostaining showed a proliferation index of 80%. Gene rearrangement analysis showed positive B lymphocyte gene IGH and IGK rearrangement in the bone marrow. Bone marrow biopsy was negative for marrow infiltration. Patient received modified CHOP chemotherapy after the surgery and was responding well. Conclusions: Accurate diagnosis of this PBL case relied on the histological morphology of the tumor cells, immunohistological markers and gene rearrangement tests. Despite the poor prognosis of PBL, surgical resection of the tumor combined chemotherapy maintains a stable state of the patient 6 months from the diagnosis. Accumulation of more cases could guide future diagnosis and treatment choices for this rare disease.

Keywords: Plasmablastic lymphoma, breast, non-Hodgkin lymphomas

Background
Plasmablastic lymphoma (PBL) is a rare entity of non-Hodgkin lymphomas which include follicular lymphoma, B-cell chronic lymphocytic leukemia, diffuse large B-cell lymphoma and other subtypes. PBL is considered a morphological variation of diffuse large B cell lymphoma [1, 2]. PBL often occurs in the oral mucosa which almost always accompanies the detection of Epstein Barr Virus (EBV) infection [3]. PBLs that involve other sites than oral cavity are rare. Here we reported a recently diagnosed case of PBL involving the breast and its pathological feature, antidiastole, treatment and prognostic factors were discussed. This will facilitate further understandings of this disease and accumulate clinical experiences for the diagnosis and treatment of PBL.
and one hypoechoic nodule above the nipple, measured 0.7×0.5 cm. These nodules had clear borders, uneven internal echo and rich blood flow signals (Figure 1). The patient was tested to be negative for HIV. Electrocardiographic examination showed she had ventricular premature beat (VPB). The patient denied any history of drinking, smoking, hypertension, cardiopathy, diabetes or cerebrovascular diseases. She denied any family history of malignancy or genetic disease but both her parents died of gastric carcinoma. The clinical diagnosis of left breast neoplasm was reached and she received surgical resection of the breast and axillary masses under general anesthesia at the end of July, 2014 after VPB was controlled. The patient reported no obvious discomfort post-surgery.

**Histologic and cytological findings**

Pathological examination showed the axillary mass to be reactive lymphoid hyperplasia. The resected breast mass measured 7×6×3 cm. A grey-white nodule was visible at the section plane, measured 1.8×1.0×1.0 cm, with unclear boundary and fine texture. Pathological examination showed heterotypic tumor cell infiltration in lymph tissues between the left nipple and left clavicle. The lobules of left mammary gland disappeared and were replaced by diffuse proliferation of tumor cells. Focal necrosis was also detected (Figure 2A). Tumor cells comprised mainly monocytes and occasionally binucleate cells. The tumor cells were large basicytes with enlarged vesicular nuclei, prominent nucleoli and numerous mitotic figures. More mature plasmocytes scattered among the large cells (Figure 2B). Immunohistochemical tests showed that the tumor cells express the plasmocyte marker VS38c (Figure 2C) and some cells were MUM1-positive. They were negative for markers CD45 (or LCA), CD20, CD79a, CD56, CyclinD1, AE1/AE3, EMA, CD30, ALK, CD117, MPO, CD38, CD138, S-100, C-myc.
Kappa, Lambda, CD68, PAX-5, HMB45, Bcl-2, Bcl-6, CD2, CD3, CD4 and CD7. Tumor cell immunostaining of Ki-67 showed a proliferation index of 80% (Figure 2D). *In situ* hybridization of EBV-EBER reported negative result. Gene rearrangement analysis of the immunoglobulin heavy chain (IGH), κ-light chain (IGK), γ-chain (IgL) and T-cell receptor β-chain (TCRB) and γ-chain (TCRG) using GeneScan fragment analysis to determine the clonality status of T cells and B cells revealed positive B lymphocyte gene IGH and IGK rearrangement in the bone marrow (Figure 3), while the TCRB Vβ-Jβ, TCRB Dβ-Jβ, TCRG Vγf/Vγ10-Jγ, TVRG Vγ9/Vγ11-Jγ clonality analysis result was negative. Based on the histological patterns, staining results and clonality assay, the pathological diagnosis of the sample was PBL in the left breast. Subsequent bone marrow biopsy was negative for marrow infiltration.

**Treatment**

The patient received 3-week radiotherapy 1.5 month after the surgery. Bilateral multiple enlarged lymph nodes in the neck were found 2.5 month post-surgery. The patient then underwent two cycles chemotherapy consisting of Epirubicin 60 mg/m² (day 1), Vincristine 2 mg (day 1), Cyclophosphamide 750 mg/m² (day 1) and Prednisone 100 mg (day 1-5) (CEOP). Drugs were well tolerated and the neck lymph node enlargement disappeared. Up to date, the patient was in good general state 5 months after the initial diagnosis.

**Discussion**

PBL most often occurs in the oral cavity but could also grow in other parts of the body. Patients are often accompanied with HIV infection or other immunodeficiencies. The appear-
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The appearance of PBL cells resembles the immunoblasts, with plasma cell differentiation. They are normally CD20 and PAX5 B-cell immune marker negative. 50%-85% of the patients express CD45, CE38, CD138, CD79a and MUM1 but not CD56 and CyclinD1 [4]. The proliferation rates are usually high (> 80%). PBL is highly invasive. Most PBL patients are also diagnosed with EBV infection with the survival time being less than 1 year [5, 6]. PBL is rarely seen involving the breast and only four cases have been reported previously [7-10] (Table 1). Including our case, the breast PBL patients aged between 36 and 56 years old. Two of the patients were HIV-positive and only one had EBV infection. Immunolabelling results of these cases showed varied results, however PAX5-, CD20-, CD79a- and CD3-negative were shared features. PBL patients tend to have very poor prognosis. Among these 5 cases, two of them died within 2 months after diagnosis. One case achieved a complete remission of the disease after numerous cycles of chemotherapy and stem cell transplantation. In our case the patient responded well to refined chemotherapy after tumor resection and is still surviving.

Definite diagnosis of PBL is important for choosing the appropriate therapeutic principles and determining prognoses. The main differential diagnosis of PBL is plasma cell myeloma (PCM) with plasmablastic differentiation. Although they share similar histological patterns and immunolabelling (both express VS38c), the
Table 1. Summary of published cases of plasmablastic lymphoma involving the breast

<table>
<thead>
<tr>
<th>Series</th>
<th>Age</th>
<th>Clinical presentation</th>
<th>HIV/EBV detection</th>
<th>Immunohistochemical findings</th>
<th>Treatment</th>
<th>Follow-up (months)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valera A et al 2010 [8]</td>
<td>42</td>
<td>Monomorphic PBL</td>
<td>+/-</td>
<td>CD45+, CD20+, CD138+, MUM1+, Clg (k)+, CD3-, CD4-, CD5-</td>
<td>NA</td>
<td>NA</td>
<td>1 DOD</td>
</tr>
<tr>
<td>Fan G et al 2014 [10]</td>
<td>53</td>
<td>NA</td>
<td>+/-</td>
<td>CD45+, CD79a+, CD38+, CD138+, MUM1+, CD20, CD56, CD10, CD30-</td>
<td>CHOP×1</td>
<td>1.9 DOD</td>
<td></td>
</tr>
<tr>
<td>Present case</td>
<td>56</td>
<td>Multiple left breast masses</td>
<td>+/-</td>
<td>VS38c+, MUM1+, CD45, CD20, CD79a, CD56, AE1/AE3, EMA, PAX5, CD30, ALK, CD38, CD138, CD2, CD3, CD4-</td>
<td>CEOP×2</td>
<td>6 AWD</td>
<td></td>
</tr>
</tbody>
</table>

NA: not applicable; COP: Cyclophosphamide, Vincristine (Oncovin®), Prednisone; CHOP: COP and Doxorubicin (Hydroxydaunomycin); CEOP: COP and Epirubicin; DOD: dead of disease; ANED: alive with no evidence of disease; AWD: alive with disease.
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In summary, herein we reported a very rare case of PBL involving the breast. We focused on the definitive diagnosis of this disease. The patient was first diagnosed with breast neoplasm and received surgical operation. Histologic examination combined cytologic analysis helped distinguishing PBL from other types of tumors. The patient responded well to chemotherapy at the time of writing. More cases need to be accumulated to instruct the diagnosis and treatment of PBL.

Ethics, consent and permissions

This study was approved by the Ethics Committee of Yantai Yuhuangding Hospital. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Disclosure of conflict of interest

None.

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