

## Case Report

# Gastric plasmablastic lymphoma: case report and review literature

Guimei Qu\*, Guohua Yu\*, Jing Liu, Di Sun, Ting Wang, Xiaolong Sui

Department of Pathology, Yantai Yuhuangding Hospital Affiliated to Qingdao University, Yantai, China. \*Equal contributors.

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**Abstract:** Plasmablastic lymphoma (PBL) is an unusual entity of non-Hodgkin lymphomas which usually occurs in the oral cavity in the immunocompromised patients. PBL involving the other sites have rarely been reported. We presented a rare case of PBL with EBV-negative in the stomach in a rheumatoid 53-year-old woman presented with stomachache for three months. During the course of gastroscopy, one giant ulcer was found. After biopsy of the ulcer, histological examinations were performed and the tumor was diagnosed as primary PBL. Tumor cells expressed CD38, CD138, CD79a, LCA, Kappa, MUM-1 and only a few neoplastic cells were CD20, CD30 and Pax-5-positive, but were negative for Bcl-6, CD10, CD3, CD56, C-myc, CK and Lambda. Ki-67 immunostaining showed a proliferation index of 80%. EBV-EBER *in situ* hybridization was negative and molecular genetic study via interphase fluorescence *in situ* hybridization did not find the rearrangement involving c-myc gene. There was no other abnormalities expect splenomegaly and atherosclerosis detected by whole body computed tomography. Bone marrow biopsy was positive for marrow infiltration. Patient received modified CHOP chemotherapy. Unfortunately, she suffered a rapid progress and died four months later after diagnosis.

**Keywords:** Plasmablastic lymphoma, stomach, non-Hodgkin lymphomas

### Introduction

Plasmablastic lymphoma (PBL) is a rare entity of B cell non-Hodgkin lymphomas which include mantle cell lymphoma, follicular lymphoma, small lymphocytic lymphoma, diffuse large B cell lymphoma and other subtypes. PBL is considered as a special morphological variation in diffuse large B cell lymphoma [1, 2]. PBL often occurs in the oral mucosa and almost accompanies the detection of Epstein Barr Virus (EBV) infection [3]. PBL in the stomach is rare and only nine cases of PBL in stomach were reported in the English literatures [4-12]. Here we reported another diagnosed case of PBL in the stomach with rapid progress and its clinic-pathological feature, differential diagnosis, treatment and prognosis were discussed with literature review. Our report will facilitate further understandings of gastric PBL and accumulate clinical experiences for the diagnosis and treatment.

### Case report

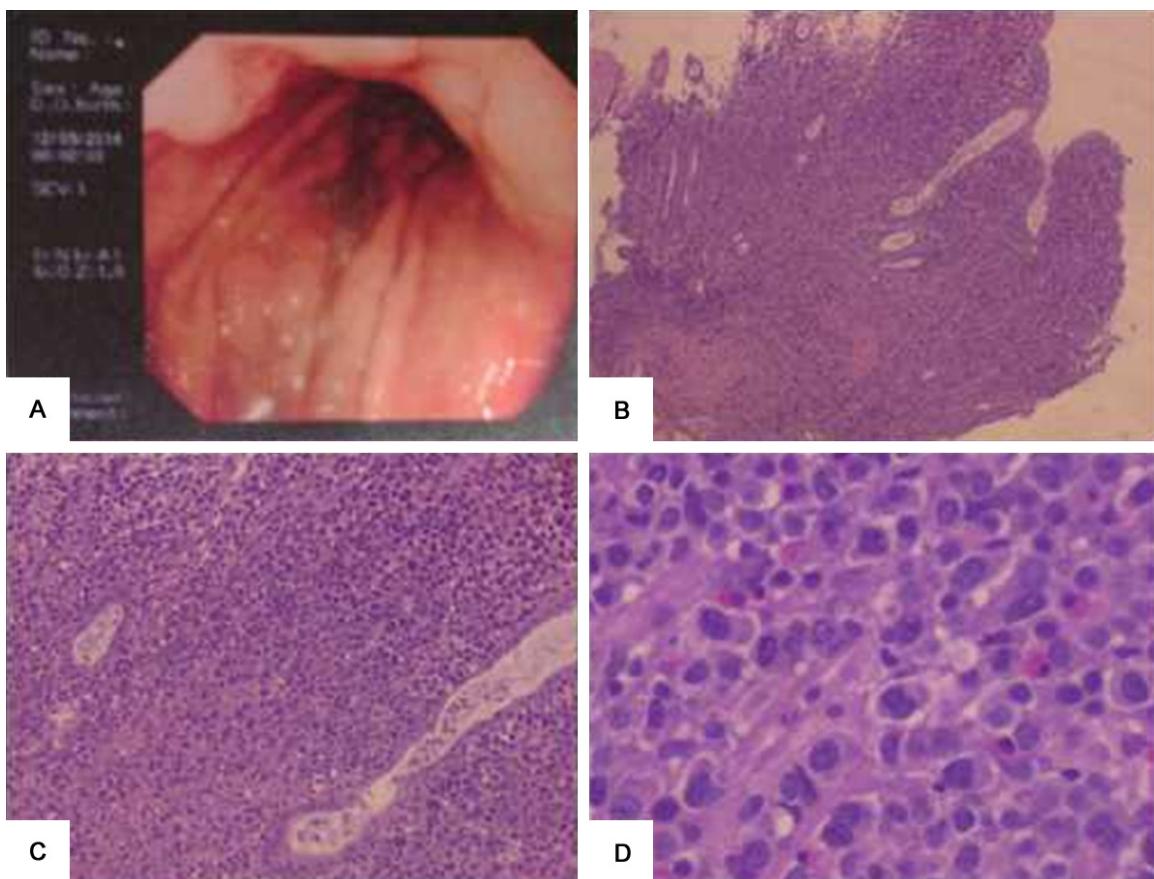
A 53-year-old woman was admitted to our Department of Gastroenterology in September

2014 due to stomach discomfort for three months. The patient had a history of connective tissue disease and take methotrexate for two years. Her temperature is 38.5 degrees celsius. Physical examination was negative for superficial lymph node. The abdominal ultrasonography revealed splenomegaly. Chest computed tomography (CT) reveal atherosclerosis. Haematological findings were: HB 73 g/L, WBC  $1.40 \times 10^9$ /L, platelets  $164 \times 10^9$ /L, CRP 124 mg/L,  $\beta$ 2-microglobulin 3.33 mg/L and Kappa 1.38 g/L. Her Five items of hepatitis B, Urine routine and anti human globulin test were within normal range. The patient denied any history of drinking, smoking, hypertension, or diabetes diseases. The patient was tested to be negative for HIV. Then, gastroscopy was carried out and one giant ulcer, area of which was about 5 cm $\times$ 2 cm, was found in gastric antrum (**Figure 1A**). Biopsy was performed subsequently.

### Histologic findings

Pathological examination showed gastric mucosa was damaged and heterotypic tumor cell infiltration in gastric mucosa (**Figure 1B** and

## Gastric plasmablastic lymphoma



**Figure 1.** Endoscopy showed one giant ulcer in gastric antrum (A). Gastric mucosa was damaged and heterotypic tumor cell infiltration in gastric mucosa (B: H&E $\times$ 40, C: H&E $\times$ 200). The tumor cells showed obvious atypia and plasmacytoid morphology (D: H&E $\times$ 400).

**1C**). 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 (**Figure 1D**). Immunohistochemical tests showed that the tumor cells expressed LCA (**Figure 2A**), CD38, CD138 (**Figure 2B**), CD79a, Kappa, MUM-1 (**Figure 2C**) and only a few neoplastic cells were CD20, CD30 and Pax-5-positive, but were negative for CK (**Figure 2D**), Bcl-6, CD10, CD3, CD56, C-myc and Lambda. Ki67 immunostaining showed a proliferation index of 80% (**Figure 2E**). *In situ* hybridization of EBV-EBER reported negative result (**Figure 2F**). Molecular genetic study via interphase fluorescence *in situ* hybridization did not find the rearrangement involving c-myc gene (**Figure 3**). Based on the clinical history, histological patterns and staining results, the pathological diagnosis of the sample was PBL in the stomach. Subsequent bone marrow biopsy was carried out and the result was positive for marrow infiltration (**Figure 4A** and **4B**).

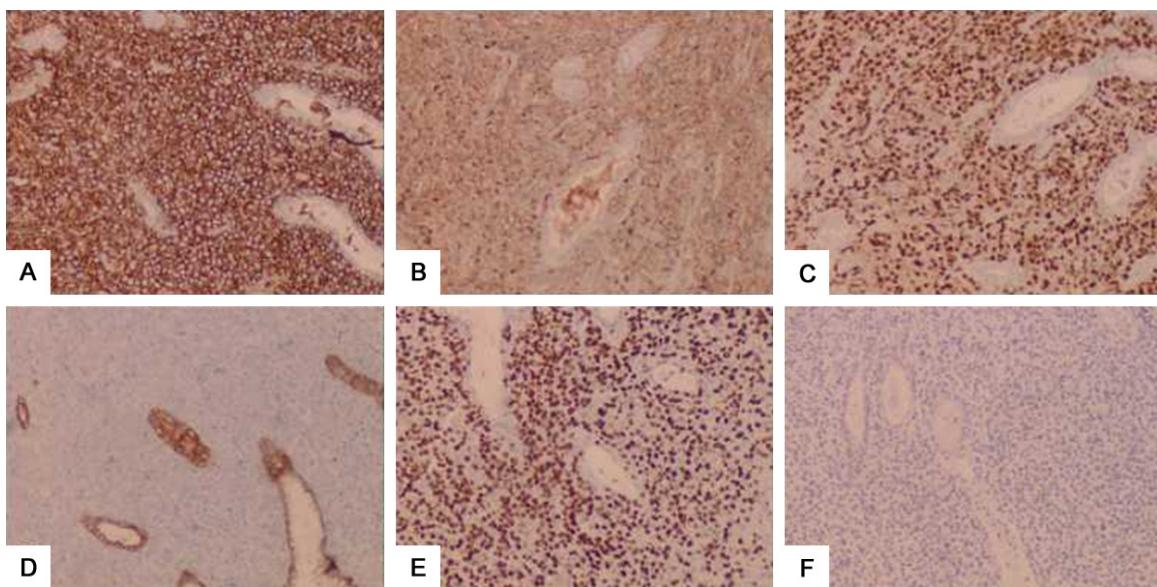
### Treatment

The patient then underwent one cycle chemotherapy consisting of Methotrexate 25 mg (Day 2, 5), Pirarubicin 40 mg (Day 1), Cyclophosphamide 0.4 (Day 1), Vindesine Sulfate 4 mg (Day 1) and Dexamethasone 10 mg (Day 1-8) (MCHOP). Unfortunately, she began suffering serious myelotoxicity and infection after chemotherapy and died in January 2015.

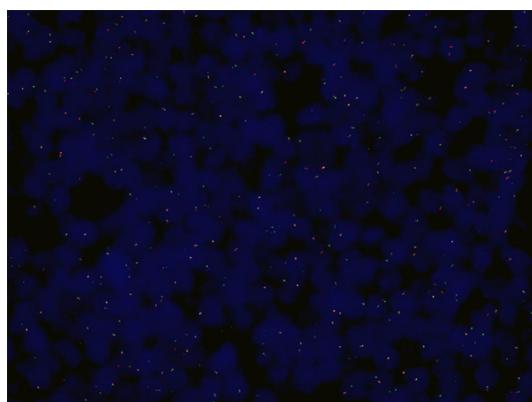
### Discussion

PBL is a rare and aggressive lymphoma in the classification of diffuse large B cell Lymphoma, which was initially described in HIV positive or immunodeficient patients. PBL is highly invasive. Most patients are also diagnosed with EBV infection and the survival time is less than one year [13, 14]. PBL most often occurs in the oral cavity associated with EBV infection, but could also grow in other parts of the body such as rectum [15], lung [16], orbits [17], breast

## Gastric plasmablastic lymphoma



**Figure 2.** Immunohistochemical study demonstrates that tumor cells are positive to CD45 (A), CD138 (B), MUM1 (C) and negative to CK (D). Proliferation index is about 80% (E) (Envision $\times$ 100). In situ hybridization staining for EBV-EBER showed the tumor cells were negative (F) ( $\times$ 100).



**Figure 3.** The rearrangement involving c-myc gene was absence detected by split gene probe( Interphase Fluorescence In Situ Hybridization).

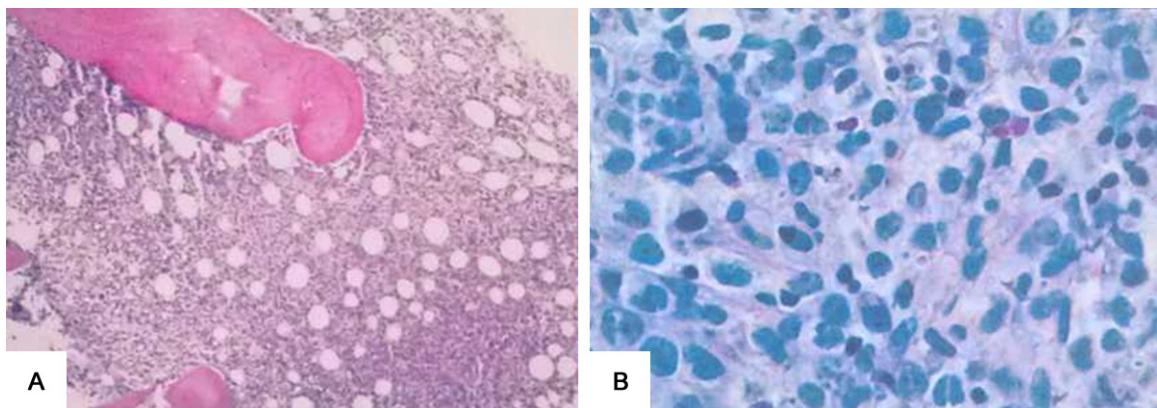
[18] and skin [19]. PBL is rarely seen involving the stomach. To the best of our knowledge, only nine cases of gastric PBL in the English literature have been reported [4-12], and the clinical information is presented in **Table 1**. Including our case, the gastric PBL patients age between 21 and 82 years old. There are seven patients over the age of 50 in the ten cases (70%, 7/10) and the median age in our group is 53 year old. There seemed to be no gender difference in gastric PBL due to male and female incidence accounted for 50%. The initial clinical manifestation of ten patients were all gastrointestinal symptoms. PBL is usually described to be close

relationship with HIV and EBV infection while PBL in the stomach do not seem to be necessary correlation because only two cases are detected with HIV and EBV infection. Consequently, our present case had a history of taking methotrexate two years for the treatment for rheumatoid and the use of immunosuppressive agents might be related to pathogenesis.

The appearance of PBL cells resembles the immunoblasts with plasma cell differentiation. They are normally not positive to CD45, CD20, PAX5 and the most patients express CD38, CD138, CD79a and MUM1 but negative to CD56 and Cyclin D1 [20]. The proliferation rate is usually over 80%. The immunohistochemical findings of ten cases are almost consistent with above information. It is worth mentioning that there are five cases positive to CD45 in eight patients in whom CD45 was detected.

Other neoplasms which are likely to be confused with diagnosis of PBL in the stomach include the plasmablastic myeloma, unspecified diffuse large B cell lymphoma (DLBCL), ALK-positive large B cell lymphoma, undifferentiated carcinoma, histiocytic sarcoma, malignant melanoma and myeloid sarcoma. Plasma-blastic myeloma can not be distinguished from PBL by morphology alone. A high ki67 index and EBV infection are preferred PBL and unusual in myeloma, while CyclinD1 and CD56 expres-

## Gastric plasmablastic lymphoma



**Figure 4.** Bone marrow biopsy showed lymphoid cells with obvious atypia infiltrated diffusely (A H&E $\times$ 100). The tumor cells were large in size with few cytoplasm, irregular nuclei and fine chromatin. The mitotic is easy to be seen(B H&E $\times$ 400).

sion are much more common myeloma and unusual in PBL. Clinical manifestation is an important basis to distinguish two disease. Paraproteinemia in blood, excess light chains proteins in urine and multiple lytic bone lesions are inclined to myeloma other than PBL [21]. In our case, the patient's extranodal pathogenic site, high proliferation index and normal immunoglobulin level confirmed the PBL diagnosis. Unspecified DLBCL is a histologic type of lymphoma mostly occurred in the digestive tract with diffuse proliferation. The neoplastic cells have similar histological morphology with PBL due to their large shapes, enlarged nuclei and prominent nucleoli. However, unspecified DLBCL abundantly expresses B-cell antigen CD20, Pax-5 while PBL does not [22]. ALK-positive large B cell lymphoma mainly affects the youth. It is mostly characterized with intranodal aggressions. Although ALK-positive large B cell lymphoma is positive for VS38c, it is unlike PBL because it is also positive to ALK and EMA [23]. Undifferentiated carcinoma is another difficult differential diagnosis with PBL due to the carcinoma cells might be recognizable as being plasmablastci in morphology and express CD-138 in protein level [24]. Occasional, PBL can even express CK in a few cases 5. However, carcinoma cells do not express CD45, MUM1 and Kappa which could distinguish from PBL. Histiocytic sarcoma cells destruct the tissue structure diffuse infiltratively. Sinus infiltration has been observed in the liver, spleen and lymph nodes. Tumor cells are large with abundant eosinophilic cytoplasm which could be confused with PBL. Histiocytic sarcoma mostly affects the extranodal intestine, skin and soft

tissue of the elderly. The cell nucleus appear circular or ovoid and lacks features for Hallmark cell nucleus. Immunohistochemistry marking shows the tumor cells are positive to CD163, but negative to VS38c, ALK, CD30, and EMA [25]. Malignant melanoma have various histologic forms with large and prominent nucleoli. Melanin granules are visible in the cytoplasm. Malignant melanoma cells express Melan A, S-100 and HMB45 in immunohistochemistry tests while PBL does not [26]. Myeloid sarcoma originates from myeloid blast cells and locates in extramedullary site. Tumor cells are positive to MPO, CD34, CD117, and negative to CD138 and VS38c which could be distinguished from PBL [27]. Therefore, the immunohistochemistry markers appear to be the major index in the diagnosis of PBL.

Definite diagnosis of PBL is important for choosing the appropriate therapeutic principles and determining prognoses. But PBL patients tend to have very poor prognosis and due to the low incidence and prevalence of the disease, no standard treatment options at present have carried out for the treatment of PBL. Therefore, common systemic chemotherapies used for lymphoma are commonly emerged for the treatment of PBL. Through the analysis of ten cases in the **Table 1**, the main treatment options for gastric PBL include EPOCH, HAART, CHOP, CVAD and DeVIC. As the rapid progresses, most of the patients died within a short period of time despite the use of chemotherapy drugs. However, it is fortunate that two patients of gastric PBL seem to get a relatively good prognosis through ProMACE-cytaBom and CVAD

## Gastric plasmablastic lymphoma

**Table 1.** Previously reported cases of plasmablastic lymphoma in the stomach

Series	Age (years)/Sex	Initial symptom	Immunohistochemical findings	HIV/EBV	c-myc rearrangement	Treatment	Follow-up Months	Status
1. Chapman-Fredricks J, et al [4]	46/Female	Nausea, vomiting, diarrhea, melena and fatigue	P: CD138, MUM1, Ki67 more than 90% N: CD45, CD20, CD79a, Pax-5, CD3, CD56, HHV-8, Kappa, Lambda	+/+	+	EPOCH, HAART	NA	NA
2. Pruneri G, et al [5]	53/Female	Epigastric distension	P: CD38, IgM, EMA, CK, Bcl-2, Ki67 about 50% N: CD45, CD20, CD19, CD79a, CD3, CD5, CD43CD56, P53, Bcl-6	-/NA	NA	ProMACE-cytaBom for six courses	19 months	NAED
3. Hashimoto M, et al [6]	70/Female	Melena and loss of appetite	P: CD138, MUM1, IgM, BOB-1, HHV-8, Ki67 about 100% N: CK, LCA, CD3, CD20, CD79a, Pax5, kappa, lambda, CD30, ALK, S-100, CyclinD1, HMB-45, MPO	-/-	NA	CHOP and DeVIC	Died during the second courses of DeVIC	DOD
4. Mihaljevic BS, et al [7]	60/Male	Abdominal pain and melaena	P: MUM1, EMA, Lambda, Ki67 about 70% N: CD20, CD3, CD38, CD138, ALK, MPO, CD34, CD117, CD56, CyclinD1, CD30, IgG, IgM, IgA	-/-	NA	CHOP	Died before the second cycle was given	DOD
5. Huang X, et al [8]	21/Male	Abdominal full-ness, diarrhea	P: CD45, CD38, MUM1, Vs38C, C-myc, Ki67 about 95% N: CK, CD20, CD79a, Pax-5, CD138, ALK, CyclinD1, CD3, CD56, Kappa, Lambda	-/-	+	no treatment	Died soon after the diagnosis	DOD
6. Riaz H, et al [9]	41/Male	Left upper quadrant abdominal pain with nausea and vomiting	P: CD45, CD43, CD19, CD38, CD138, IgG, Kappa, Ki67 was not checked N: CD3, CD20, CD56, Kappa, CK, CyclinD1	-/NA	NA	Cyclophosphamide 600 mg/m <sup>2</sup> , doxorubicin 50 mg/m <sup>2</sup> , vincristine 2 mg, methotrexate for CNS prophylaxis	NA	NAED
7. Angeleri A, et al [10]	50/Male	Fatigue, weakness, weight loss, impaired general condition and increased abdominal girth	P: CD45, CD38, CD138, Ki67 about 100% N: CD3, CD20, CD56, CD79a, Pax-5	+/+	NA	NA	NA	NA
8. Kim JE, et al [11]	61/Male	NA	P: CD45, Ki67 about 70% N: CD20, Pax-5, MUM1, CD10, CD56, Bcl-6, CK, ALK, CyclinD1	-/-	NA	Surgery	3 months	DOD
9. Marques I, et al [12]	82/Female	Melena, epigastric pain, and progressive abdomen fullness	P: CD138, MUM1, Kappa N: CD45, B-cell associated antigens	-/NA	NA	CHOP	Died before the second cycle	DOD
10. Present case	53/Female	Stomachache	P: CD45, CD38, CD138, CD79a, Kappa, MUM1 N: Bcl-6, CD10, CD3, CD56, C-myc, CK, Lambda	-/-	-	MCHOP	4 months	DOD

Abbreviations: P: positive; N: negative; NA, not applicable; ANED, alive with no evidence of disease; DOD: died of disease.

## Gastric plasmablastic lymphoma

with CNS prophylaxis respectively. Recently, some scholars speculated that CD45 expression and/or EBV infection could predict a better outcome, meanwhile c-myc gene abnormality was associated with an adverse prognosis in PBL [8, 28]. Nevertheless, Three patients with CD45 positive died among four patients who get the follow-up data judging from the information of **Table 1**, and CD45 expression do not seem to be a indicator for better prognosis. Although c-myc gene rearrangement did not be detected in our present case, she still experienced a rapid progress and died four months later. Certainly, it is necessary to accumulate much more gastric PBL cases to confirm the prognostic indicator.

In summary, herein we reported an usual case of PBL in the stomach and relative literature was reviewed. Gastric PBL is an aggressive neoplasm. We focused on the definitive diagnosis of this disease and histological examination combined with immunohistochemical staining helped distinguishing PBL from other types of tumors. There is no specific treatment for gastric PBL at present. More cases need to be accumulated to instruct the diagnosis and treatment of gastric PBL in the future.

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### Disclosure of conflict of interest

None.

**Address correspondence to:** Guimei Qu, Department of Pathology, Yantai Yuhuangding Hospital Affiliated to Qingdao University, Yantai 264000, China. E-mail: guimeiqu@sohu.com

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## Gastric plasmablastic lymphoma

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