Plasmablastic Lymphoma of the Stomach With C-MYC Rearrangement in an Immunocompetent Young Adult
A Case Report
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Abstract: Plasmablastic lymphoma (PBL) is a rare B-cell neoplasm mostly described in human immunodeficiency virus–infected patients. Herein, we described a case of PBL presenting as gastric mass in a 21-year-old young adult without known immunodeficiency. The histological examination of the specimen showed a diffuse proliferation of round- to oval-shaped large cells with scant cytoplasm, and prominent nucleoli. The neoplasm stained positively for CD45, CD38, MUM1, and Vs38C, but typical B-cell and T-cell markers (PAX5, CD20, CD79a, and CD3) were absent. The proliferative index (Ki-67) was about 95%. And the neoplastic cells diffusely expressed the c-myc protein. Epstein–Barr virus–encoded RNA in situ hybridization was negative. Molecular genetic study via interphase fluorescence in situ hybridization disclosed the rearrangement involving c-myc gene.

Awareness of this distinctive lymphoma can prevent misdiagnosis by the clinicians and/or the pathologists.

INTRODUCTION
Plasmablastic lymphoma (PBL) was first described as a human immunodeficiency virus (HIV)–related lymphoma with an almost exclusive involvement of oral cavity. However, many case reports have been published describing PBL of HIV-negative individuals. In the 2008 World Health Organization (WHO) classification, PBL was designated as a distinct entity of B-cell lymphoma. Histologically, PBL mainly displayed two forms based on the presence or the absence of neoplastic plasma cells in the background, namely PBL with plasmacytic differentiation and monomorphic PBL. The phenotype of PBL is that of a terminally differentiated B-cell phenotype characterized by the loss of mature B-cell markers and the expression of plasma cell–related antigens. Although the exact pathogenesis of PBL remains unclear, recent studies have reported Epstein–Barr virus (EBV) infection and/or the dysregulation of c-myc gene to be the potential pathogenic factors in the development of PBL, particularly in the HIV-positive patients. Clinically, it’s highly aggressive, often rapidly fatal, and due to its rarity, there are no specific therapies for PBL. Awareness of this rare and unique lymphoma is important to prevent the misdiagnosis. Currently, we reported a primary gastric PBL with c-myc gene rearrangement which suffered a rapidly progressive clinical deterioration and died within 2 weeks.

CASE REPORT
A 21-year-old young adult complained of abdominal fullness, diarrhea, and an increase in abdominal girth for 1 week. Serum lactate dehydrogenase level was elevated, and HIV serology was negative. The bone marrow aspirate was unremarkable. An abdominal ultrasound confirmed the accumulation of free-flowing ascites in the abdominal cavity. An endoscopic examination of the upper gastrointestinal tract revealed a large gastric polyloid mass from which biopsy was taken. Whole-body computed tomography revealed no other abnormalities. Microscopically, the specimen of the gastric mass showed a monotonous proliferation of large cells with prominent nucleoli and scant cytoplasm. The tumor stained positively for CD45, CD38, MUM1, and Vs38C. The proliferative index (Ki-67) was over 95%. The EBV in situ hybridization was negative. Expression of c-myc protein was detected in almost all tumor cells, consistently with the result of FISH analysis, which further confirmed the translocation involving the c-myc gene. The clinicopathological features of our case were consistent with those of PBL described in the 2008 WHO classification. Additionally, a diagnostic paracentesis was performed and the cytological analysis of ascitic fluid cells revealed the presence of large atypical cells with morphological features similar to those seen in the gastric biopsy. The patient did not receive any treatment because he suffered a rapid clinical progression and died soon after the diagnosis.

MATERIALS AND METHODS
Ethical approval was not required for this case report as it did not relate to patient’s privacy or treatment.

Morphologic and Immunophenotypic Studies
Formalin-fixed paraffin-embedded tissue block of tumor mass specimen from this patient was obtained. Histological evaluation was done with hematoxylin and eosin stained section.
Immunohistochemistry was performed using the EnVision system (DAKO, CA). The lesion was stained for the following markers: CKpan, CD45, CD20, CD79a, PAX5, CD3, CD56, CD38, CD138, MUM1, Vs38C, kappa, lambda, c-myc, cyclin D1, ALK1, HMB45, and Ki-67.

In situ hybridization
Detection of EBV in tumor cells was performed by in situ hybridization (ISH) on paraffin sections with a fluorescein-conjugated PNA probe specific for the EBV-encoded EBER RNAs (DAKO, Glostrup, Denmark). A known EBV+ tissue section was used as a positive control.

Fluorescence In situ Hybridization
Fluorescence in situ hybridization (FISH) was performed on paraffin section according to the manufacturer’s instructions (Vysis/Abbott Molecular) with minor modifications. Commercially available c-myc dual color break-apart probe (Vysis/Abbott Molecular) was used to look for c-myc gene rearrangement.

RESULTS

Histopathological Findings
Histologically, the gastric mucosa was extensively infiltrated by monomorphic large atypical cells with round pale nuclei containing large central nucleoli and abundant amphophilic cytoplasm (Figure 1A), resembling plasmablasts or immunoblasts. Apoptotic bodies and mitotic figures were numerous.

Immunohistochemical Findings
The tumor cells stained strongly for plasma cell markers, that is, CD38 (Figure 1C), MUM1 (Figure 1D), and Vs38C. CD45 (Figure 1B) was also positive but the staining was relatively weak. Negative markers included AE1/AE3, CD20, CD79a, PAX5, CD138, ALK1, cyclin D1, CD3, CD56, kappa, lambda, and HMB45. The Ki-67 index was nearly 95% (Figure 1E). And the neoplastic cells expressed the c-myc protein (Figure 1F).

FISH Analysis
FISH analysis identified the translocation involving the c-myc gene. Figure 1G demonstrates clearly separated green and red signals. The normal c-myc gene signal is shown as a fused yellow signal or joined green and red signals.

DISCUSSION
PBL is a very rare disease entity that usually poses great diagnostic and treatment challenges. The current case was a primary gastric lymphoma of a HIV-negative, immunocompetent patient with morphologic and phenotypic features of PBL. PBLs most often occur in HIV-infected patients or those in immunocompromised or immunosuppressive status. Oral cavity is the most common site of extranodal involvement in PBL, followed by gastrointestinal tract. PBLs are reported to be frequently associated with EBV infection, particularly in the HIV-positive cases. In the HIV-negative PBLs, the majority of EBV-positive cases arose in the nasal cavity whereas cases occurring in the gastrointestinal tract were usually EBV-negative. As expected, our case was also EBV negative.
The histological appearance of the current case may also be suggestive of undifferentiated carcinoma or melanoma. However, the negativity for AE1/AE3, HMB45, and S-100 by immunohistochemistry helped rule out the above considerations. The neoplasm displayed a plasma cell phenotype expressing CD38, Vs38C, and Mum1 but negative for pan-B cell antigens including CD20, PAX5, and CD79a. Furthermore, the absence of ALK1 expression excluded ALK-positive large B-cell lymphoma. Thus, the overall clinicopathologic feature of the present case is that of PBL.

Previous studies suggested that \textit{c-myc} gene abnormalities were the most common recurrent cytogenetic alteration in PBL, encountered in over half of cases.6,8 As predicted, we also observed the \textit{c-myc} gene rearrangement by FISH analysis in this case.

A recently published meta-analysis proposed that CD45 expression, EBV positivity, or the combination of both parameters all predicted a better outcome, whereas \textit{c-myc} gene abnormality was associated with an adverse prognosis in PBL.9 As mentioned earlier, our patient experienced an extremely aggressive clinical course and died soon after diagnosis. It’s notable that this case demonstrated CD45 immunoreactivity, the absence of EBV infection, and the presence of \textit{c-myc} gene rearrangement. It suggests that \textit{c-myc} gene abnormality may exert an even stronger influence on predicting the prognosis of PBL. However, this needs to be confirmed on larger and prospective series.

In conclusion, PBL is an extremely rare neoplastic lesion of the stomach. There are no specific symptoms and radiologic imaging. Definite diagnosis depends on histopathology and immunohistochemical stains.

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