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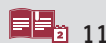
# Primary Isolated Lymphoplasmacytic Lymphoma (LPL) of the Stomach: A Case Report

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Conflict of interest:** None declared**Patient:** Male, 47-year-old  
**Final Diagnosis:** LPL of the stomach  
**Symptoms:** Reflux symptoms  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Oncology**Objective:** Rare disease**Background:** Lymphoplasmacytic lymphoma (LPL) is a mature B cell lymphoma that mostly involves the bone marrow, spleen, and lymph nodes. Involvement of extramedullary sites is very rare and has not been reported as the primary site before.**Case Report:** A 47-year-old man presented with reflux symptoms. Gastroscopy revealed a 1.5-cm gastroesophageal junction (GEJ) polyp and oesophageal ulcer. A biopsy was performed and histopathology showed active chronic inflammation with focal intestinal metaplasia and reactive epithelial changes. A CT abdomen showed eccentric thickening of the lower oesophagus and GEJ, with periesophageal, gastro-hepatic ligament, and coeliac lymph node (LN) enlargement. A laparoscopic biopsy showed no peritoneal disease. EUS showed a large ulcerated lesion in the GEJ and proximal stomach. Both were biopsied, showing squamous-columnar mucosa with edema and a population of plasma cells, small lymphocytes, and histiocytes. These expressed CD20, PAX5, CD79a, IgM, and were lambda light chain-restricted. Lymphocytes were negative for CD3, IgG, IgA, and IgD. The MIB-1 index was low. LPL was diagnosed. PET showed an increased uptake of the gastric cardia and GEJ. LNs were not metabolically active. Bone marrow was negative. Evaluation of MYD 88 mutational status failed. Serum immunofixation showed no paraprotein. These results led to a diagnosis of primary isolated LPL of the stomach.**Conclusions:** Primary lymphoplasmacytic lymphoma may present as an isolated gastric tumor. This can be unassociated with a paraprotein in serum and increased lymphocyte/plasma cell populations within the bone marrow. Gastric LPL is rare. Physicians and pathologists need to be aware of this rare presentation.**MeSH Keywords:** Gastrointestinal Neoplasms • Lymphoma, Non-Hodgkin • Stomach Neoplasms**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/921840>

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## Background

Lymphoplasmacytic lymphoma (LPL) is a rare type of non-Hodgkin lymphoma that is characterized by infiltration of small B lymphocytes, plasmacytoid lymphocytes, and plasma cells. The condition most commonly affects the bone marrow, followed by lymph nodes and spleen, and, to a lesser extent, the lung or gastrointestinal (GI) system. Typically, LPL is associated with monoclonal IgM paraprotein secretion of  $>3$  g/dL [1].

Herein, we report a case of LPL with exclusive presentation as an extra-medullary lesion within the gastroesophageal junction (GEJ).

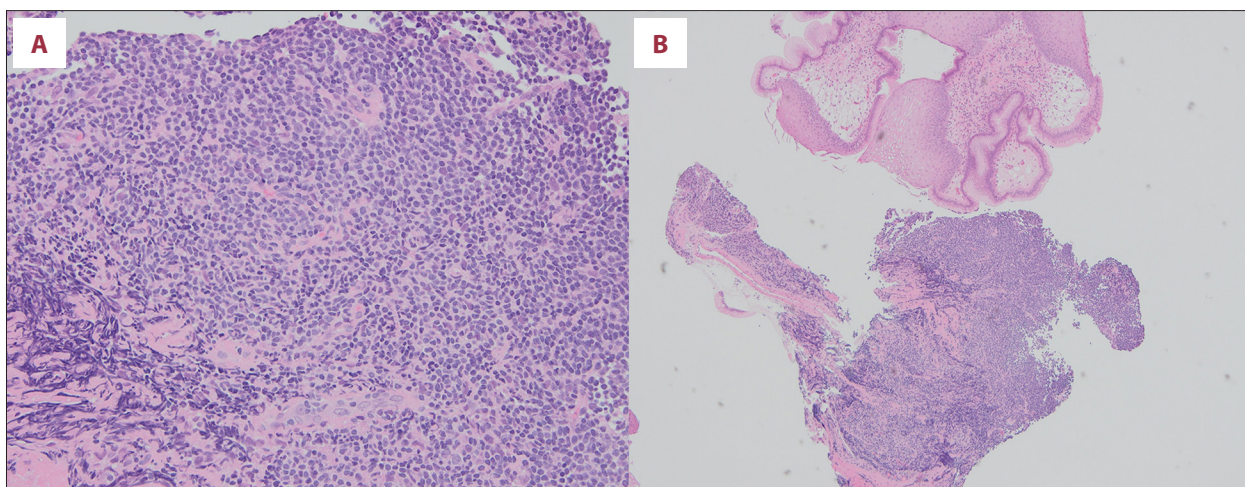
## Case Report

A 47-year-old man presented with reflux symptoms. There was no history of hematemesis, fever, night sweats, chills, or loss of weight. Past medical history was non-contributory. He had a family history of prostatic carcinoma (father) and breast cancer (mother). He was a lifetime non-smoker, with alcohol intake of 4 units per week. Otherwise, the physical examination was unremarkable. Laboratory testing showed a white blood cell count of  $6.2 \times 10^3$ /dL, hemoglobin 15.2 g/dl, platelet count  $228 \times 10^3$ /dL, serum sodium 140 mmol/L, potassium 4.2 mmol/L, creatinine 0.79 mg/dl, estimated GFR 91 mL/min, calcium 2.36 mmol/L, bilirubin total 0.8 mg/dl, ALP 97 mg/dl, total protein 6.9 g/dl, albumin 4.6 g/dl, and lactate dehydrogenase (LDH) 174 U/L. Plasma viscosity was normal. HBV, HCV, and HIV were all negative.

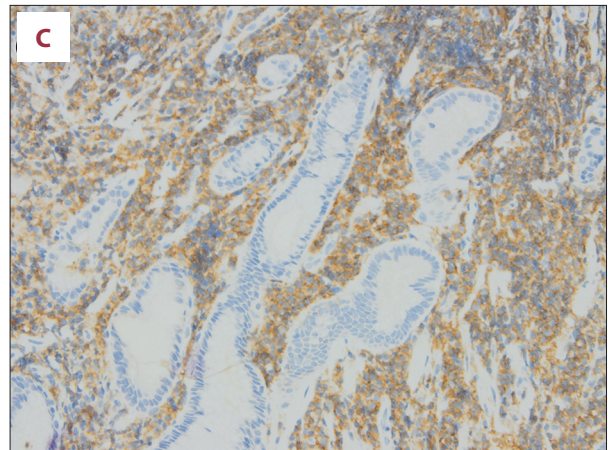
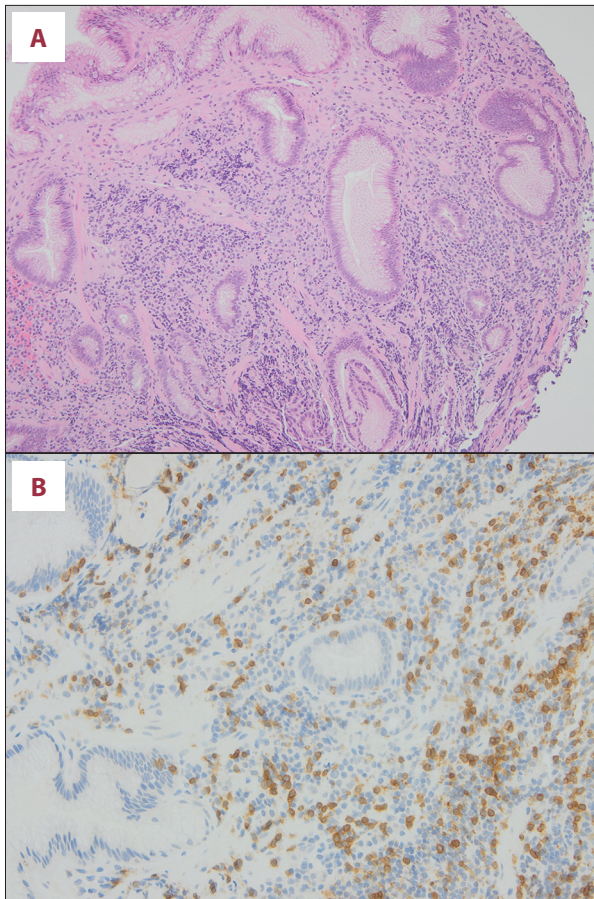
A CT scan confirmed a hiatus hernia and raised the suspicion of a neoplastic gastric lesion along with lymphadenopathy. Staging laparoscopy revealed an abnormal lesion – type

2/3 disease. A biopsy was performed, but no peritoneal disease was found. EUS showed a large ulcerated lesion extending from the SJC to the proximal stomach on lesser curvature type III. Both were biopsied. Histopathology showed squamocolumnar mucosa with a population of submucosal plasma cells, lympho-plasmacytoid cells, small lymphocytes, and histiocytes. On immunohistochemistry, these expressed CD20, PAX5, CD79a, and IgM, and were lambda light chain-restricted. The lymphocytes were negative for CD3, cyclin D1, IgG, IgA, and IgD (Figure 1). The MIB-1 labelling index was low ( $<5\%$ ). FISH showed no evidence of IGH-MALT or BIRC3 (API2)-MALT rearrangements. Tests for MYD 88 mutational status failed. Multiple additional gastric biopsies did not show a tumor or evidence of *H. pylori*-like organisms or chronic active gastritis. Lymphoplasmacytic lymphoma was diagnosed. PET showed an intensely increased uptake of tracer centered on the gastroesophageal junction and gastric cardia extending along the lesser curvature, with SUV max=8.5. The subcentimeter left gastric LN (at least 3 seen) and para-esophageal LN were not metabolically active. A bone marrow biopsy did not reveal lymphoma. Serum immunofixation showed normal-range immunoglobulin levels. These findings together indicated a diagnosis of primary isolated LPL of the stomach.

Following discussion in the multidisciplinary team, radical radiotherapy was agreed upon. VMAT technique radiotherapy to a total dose of 24 Gy in 12 fractions, including the whole stomach as the clinical target volume, was given (Figure 2). Treatment was very well tolerated with no grade  $\geq 2$  toxicity. A repeat PET/CT 3 months after radiotherapy showed a complete metabolic response (Figure 3).



**Figure 1.** Gastroesophageal biopsy showing H&E staining of submucosal tumor composed of lymphocytes and plasma cells. (A) 20 $\times$  and (B) 10 $\times$ .



**Figure 2.** Gastroesophageal biopsy showing transitional mucosa with no evidence of lymphoepithelial lesion (LEL) on CD staining and normal number of intraepithelial CD3 cells. (A) H&E, (B) CD20 with no LEL, and (C) CD3 intraepithelial lymphocytes.

to a lesser extent, the lungs or GI system. Most patients either remain asymptomatic or present with anemia [7].

The involvement of GI tract in IPL occurs secondarily to extensive nodal disease, while primary GI lymphoma is a rare malignancy that is seen in less than 4% of all cases of GI tumors. Patients with GI lymphoma usually present with a wide range of non-specific symptoms such as progressive weight loss, bowel irritation, epigastric pain, and vomiting [8]. The diagnosis of primary GI lymphoma is usually based on the 5 criteria developed by Dawson, which are: (i) no palpable lymphadenopathy; (ii) no mediastinal lymphadenopathy; (iii) normal leucocytic count; (iv) the lesion is mainly confined to the bowel in laparotomy with lymph nodes involvement limited lesion area only; and (v) free liver and spleen [9].

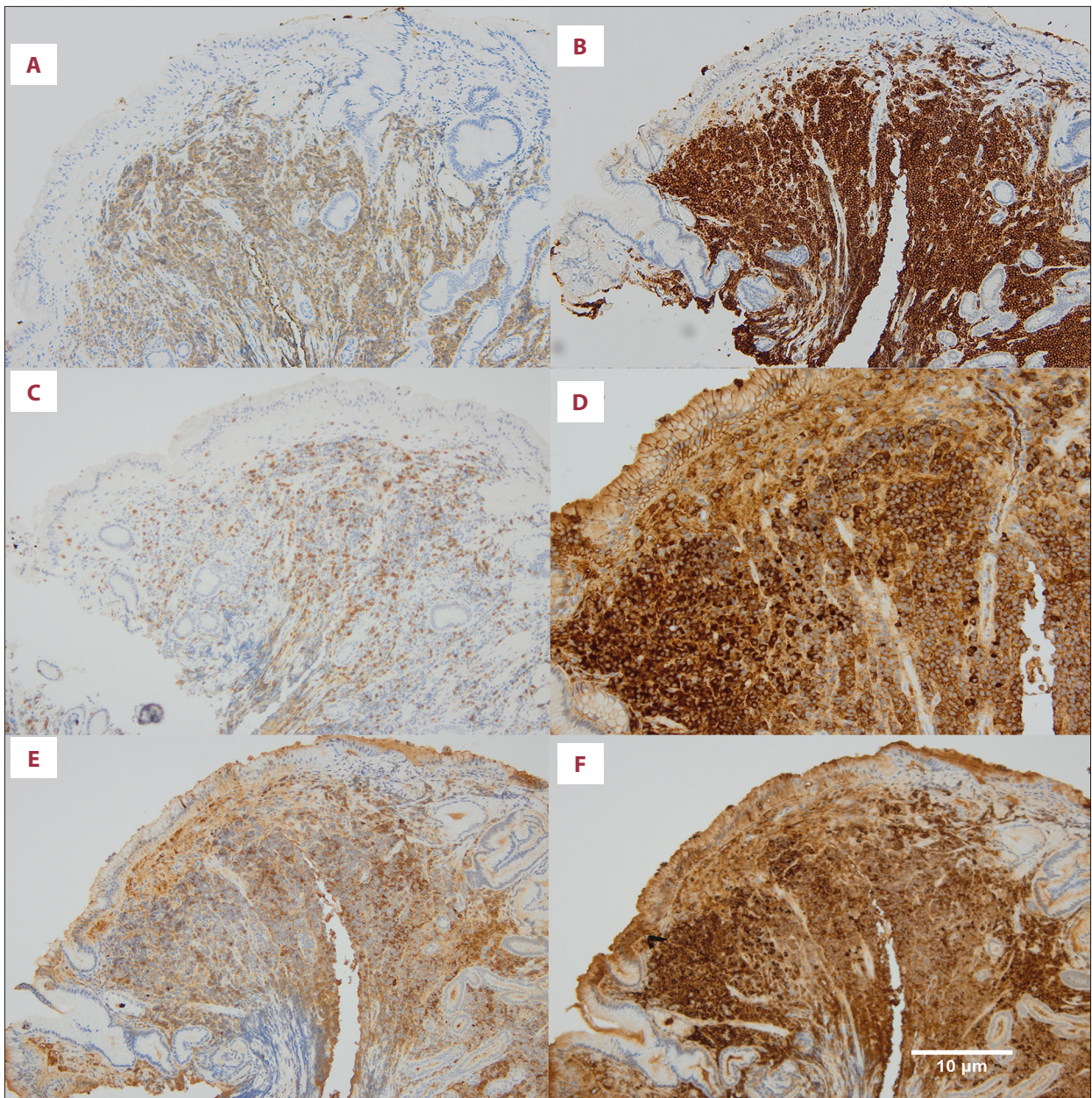
Histopathologically, the differential diagnosis of low-grade lymphomas with plasmacytic differentiation at this site revolves around exclusion of an extra-nodal mucosa associated marginal zone lymphoma. Morphologically, this presents with lymphoepithelial lesions and a largely centrocytic/monocytoid lymphoid infiltrate admixed with plasma cells. FDC meshworks are usually clearly visible on CD21/CD23 staining, and this is invariably associated with a *H. pylori*-associated chronic active gastritis. None of these features were seen in our case. While MALT lymphomas with a predominantly plasmacytic morphology have been described, the features in our case are more in keeping with LPL. The lack of background gastritis, absence of HLO, location centered around the GOJ, and absence of MALT-associated genetic abnormalities also favors a diagnosis of LPL.

Deletions of 6q21 were identified as a common genomic event in patients with WM. This suggested that MYD88 mutations,

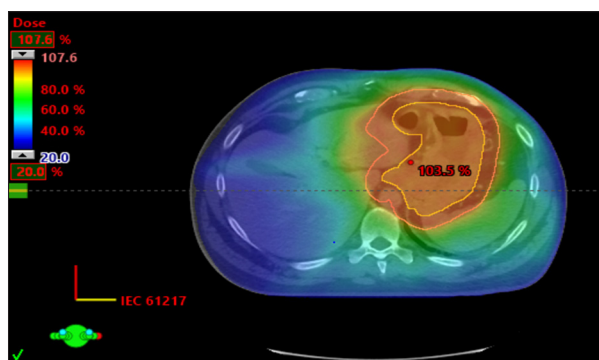
## Discussion

LPL is a rare type of B cell lymphoma that accounts for less than 1% of new cases of hematologic malignancies [1]. Previous epidemiological studies showed that LPL affects almost 8 cases per 1 000 000 population every year in the United States and Western Europe [2,3]; however, data from Asia showed a notably higher incidence of LPL than in the United States (up to 10-fold higher) [2]. LPL usually affects the elderly population (median age=65 years) with a male predominance. In addition, the incidence of LPL shows a racial difference, with the majority of cases being white [4].

While the pathogenesis of IPL is not fully understood, previous reports suggested that genetic alterations and chronic viral infections (e.g., HIV and HCV) are risk factors for IPL [5]. In many cases of LPL, the marrow infiltration is associated with excessive secretion of serum monoclonal IgM. This combination is known as Waldenström's macroglobulinemia (WM), a distinct subtype of LPL according to the 2008 World Health Organization (WHO) classification. Although the vast majority of IPL patients present with WM, IPL is rarely associated with increased secretion of IgA or IgG [6]. IPL most commonly affects the bone marrow, followed by lymph nodes and spleen, and,



**Figure 3.** Immunohistochemistry: (A) CD20, (B) CD79a, (C) CD3, (D) IgM, (E) Kappa, and (F) Lambda.



**Figure 4.** VMAT technique radiotherapy plan dose wash.

which activate the NF- $\kappa$ B family transcription factors, play a crucial role in the evolution of LPL [6]. In their report, Treon et al. identified a somatic variant (T→C) in MYD88 gene in the majority of patients with MW [10]. Subsequently, many studies have reported a high prevalence (80–100%) of the MYD88 L265P mutation in LPL/WM compared to a low prevalence in other NHLs. In 2016, testing for MYD88 was added to the recommendations for initial work-up of LPL/WM in the NCCN Guidelines. Recent studies have suggested the role for MYD88 L265P in cellular growth signaling pathways, most notably Bruton Tyrosine Kinase (BTK), which can be targeted by therapy against BTK (e.g., ibrutinib) [11]. MYD88 testing unfortunately failed in our case.

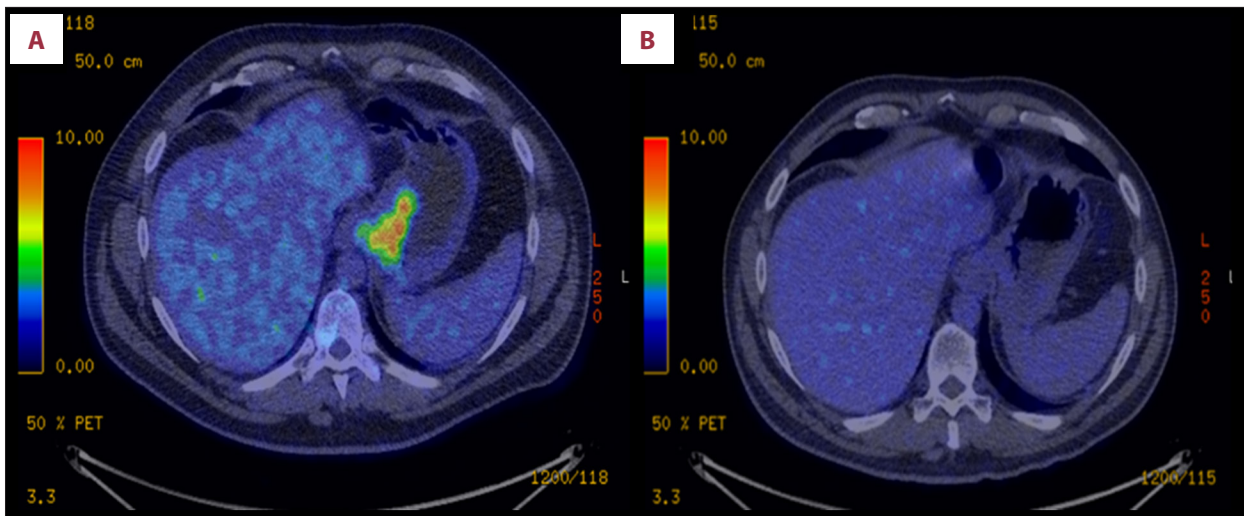


Figure 5. PET/CT scan: (A) Pre-treatment and (B) Post-treatment.

## Conclusions

Our review of the literature shows that this is the first documented case of a primary isolated lymphoplasmacytic lymphoma of the stomach.

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## Conflict of interest

None.