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Clinical and Endoscopic Features of Primary Gastrointestinal Lymphoma in A Guatemalan Cohort: A Case Series from Igss

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1. Abstract

1.1. Background

Primary gastrointestinal lymphoma (PGIL) is an uncommon but clinically significant malignancy, often presenting with nonspecific gastrointestinal symptoms that delay diagnosis. General objective: To describe the clinical, endoscopic, and histopathologic features of PGIL in patients treated at a tertiary centre in Guatemala.

1.2. Methods

We conducted a retrospective, descriptive, single-centre study of patients diagnosed with diffuse large B-cell lymphoma (DLBCL) or mucosa-associated lymphoid tissue (MALT) lymphoma at the Guatemalan Social Security Institute (IGSS) from January 2023 to January 2025. Variables analysed included demographics, symptoms, endoscopic features, histopathology, Helicobacter pylori status, treatment, and outcomes.

1.3. Results

A total of 11 patients were included, with 90.9% DLBCL and 9.1% MALT. Median age was 57 years; 90.9% were male. The most common symptoms were upper GI bleeding (54.5%) and abdominal pain (45.5%). The gastric antrum (36.4%) and small bowel (27.3%) were the most frequent locations. H. pylori was detected in 45.5% of patients. Most received R-CHOP (54.5%), with adjuvant surgery in 36.4%. Mortality was 36.4%, associated with younger age, upper GI bleeding, high-grade histology, elevated Ki-67, and advanced stage.

1.4. Conclusion

PGIL shows heterogeneous clinical and endoscopic features, often associated with H. pylori infection. Timely diagnosis and multidisciplinary management are essential to improve prognosis.

2. Introduction

Primary gastrointestinal lymphoma (PGIL) is a rare malignancy that can involve any segment of the digestive tract, from the oropharynx to the rectum. It accounts for approximately 5% of primary gastrointestinal neoplasms and represents the most common type of extranidal lymphoma, comprising 4% to 20% of all extranidal lymphomas [1]. According to the World Health Organization (WHO), the most frequent histologic subtypes are diffuse large B-cell lymphoma (DLBCL), a high-grade lymphoma, and mucosa-associated lymphoid tissue (MALT) lymphoma, a low-grade neoplasm [2-4]. Gastric MALT lymphoma has a strong association with Helicobacter pylori infection, and early-stage cases may achieve complete remission after eradication therapy in up to 80% of patients [4]. Beyond the stomach, other GI segments can be affected. Mantle cell lymphoma is more frequent in the ileum, enteropathy-associated T-cell lymphoma in the jejunum, and follicular lymphoma in the duodenum. In the colon, lymphomas are uncommon and often appear as ulcerated or obstructive tumours [5,6]. The clinical presentation of PGIL is diverse, ranging from nonspecific symptoms such as dyspepsia, abdominal pain, and weight loss to serious complications like gastrointestinal bleeding, perforation, or intestinal obstruction. This clinical variability may lead to delayed diagnosis, highlighting the importance of appropriate endoscopic and clinical evaluation [7-9]. In Guatemala, specific epidemiologic data on PGIL are lacking. However, the high prevalence of H. pylori in gastric cancer (78.8%) suggests a

strong epidemiologic association with gastric MALT lymphoma, which is linked to H. pylori in over 90% of cases [8]. Diagnosis is based on upper GI endoscopy or colonoscopy with biopsies, supported by histopathology and immunohistochemistry. Endoscopic appearance is variable ranging from ulcers and raised lesions to fold thickening or tumour masses making differentiation from other GI neoplasms challenging [10-12]. Treatment depends on histologic subtype, stage, and H. pylori status. While early-stage gastric MALT lymphoma may respond to antibiotic eradication, gastrointestinal DLBCL typically requires R-CHOP chemotherapy. More aggressive therapies, including intensive chemotherapy and stem cell transplantation, may be needed in mantle cell lymphoma or T-cell lymphoma. In advanced cases, radiotherapy and palliative surgery may be indicated to control symptoms and improve quality of life [13-17].

3. Materials and Methods

A retrospective, single-centre study was conducted at the Guatemalan Social Security Institute (IGSS) from January 2023 to January 2025. Patients with histologically confirmed diagnoses of diffuse large B-cell lymphoma (DLBCL) or mucosa-associated lymphoid tissue (MALT) lymphoma were included. Clinical, histopathologic, and endoscopic data were extracted from medical records and the Pathology Department database. Epidemiologic, clinical, biochemical, and endoscopic features were documented. Symptoms were categorized as "alarm" or "non-alarm" according to European guidelines. Histologic classification followed De Jong criteria, distinguishing low-grade (MALT) from high-grade (DLBCL) lymphomas. Immunohistochemistry with CD20 and CD3 staining was used to determine cell lineage, and staging was performed using the Lugano classification. Additional biomarkers included haemoglobin, albumin, and lactate dehydrogenase (LDH). Bone marrow biopsies were reviewed for hematopoietic infiltration. Helicobacter pylori status was assessed via histologic analysis of gastric mucosa. Endoscopic findings were categorized as ulcerative, exophytic, hypertrophic, or petechial haemorrhagic lesions, with detailed documentation of anatomical distribution and morphological characteristics. This was a descriptive, observational study. Numerical variables were analysed using measures of central tendency (mean, median) and dispersion (standard deviation, interquartile range). Categorical variables were presented as absolute frequencies and percentages. Due to the descriptive nature of the study and sample size limitations, no multivariate or causal inference analyses were performed.

4. Results

A total of 11 patients diagnosed with diffuse large B-cell lymphoma (DLBCL) or mucosa-associated lymphoid tissue (MALT) lymphoma were included. All were treated at the Guatemalan Social Security Institute (IGSS). Table 1 summarizes the clinical and demographic characteristics of the cohort. The mean age was 57.18 years (SD: 18.68), with a marked male predominance (90.9%, n=10). The most common presenting complaints were upper gastrointestinal bleeding (UGIB) in 54.5% (n=6) and abdominal pain in 45.5% (n=5). Symptom duration before diagnosis ranged from 3 to 20 days, with a median of 7 days. The most frequent anatomical locations of the lymphoma were the gastric antrum (36.4%, n=4) and the small intestine (27.3%, n=3), followed by the gastric body, fundus, and cardia. Helicobacter pylori infection was detected in 45.5% (n=5) of cases; in the remaining patients, the test was either negative or not performed. Regarding treatment, the most commonly administered chemotherapy regimen was R-CHOP (54.5%), followed by alternative regimens including R-DA-EPOCH, POLA/B-CHOP, and CHOP. Two patients (18.2%) underwent adjunctive surgery (partial gastrectomy or intestinal resection). The median follow-up duration was 4 months (range: 1–12 months). The overall mortality rate was 36.4% (n=4), primarily in patients with high-grade lymphomas and those who presented with UGIB Table 1. The deceased patients had a mean age of 47.25 years (SD: 13.12), whereas survivors had a higher mean age of 62.85 years (SD: 19.81). All deceased patients were male (100%), compared to 85.7% male and 14.3% female in the survivor group. Most patients presented with advanced-stage disease (stage > I: 90.9%), with similar distribution between both groups. Regarding clinical symptoms, melena and anaemia were observed in 25% of deceased patients and 28.6% of survivors Table 2. Endoscopic findings revealed ulcerative lesions in 18.2% of cases, with a similar distribution between deceased and surviving patients. The most frequent location was the gastric antrum (36.4%), found exclusively in survivors (57.1%), while the small intestine (27.3%) was more common among deceased patients (50%). Helicobacter pylori was positive in 45.5% of cases, with a higher prevalence among survivors (57.1% vs. 25%). DLBCL was diagnosed in 90.9% of patients, with no differences between groups. The markers CD20 (100%), BCL6 (90.9%), and C-MYC (90.9%) were positive in most cases. The KI-67 index was higher in deceased patients (80.75% vs. 75.71% in survivors) Table 3. 45.5% of patients received chemotherapy alone, while another 45.5% underwent combined chemotherapy and surgery, with distributions of 50% and 25% among deceased patients, and 42.9% and 57.1% among survivors, respectively. The most commonly used chemotherapy regimen was R-CHOP (36.4%), followed by CHOP, POLA-R-CHOP, R-MINI CHOP, and POLA-R-BENDA (9.1% each), with a single case of POLA-R-BENDA (25%) among the deceased group. Regarding surgery, intestinal resection (36.4%) and partial gastrectomy (18.2%) were performed, with higher proportions among survivors (42.9% and 28.6%, respectively). The mean disease course duration was 4.9 months (SD: 3.96), with no significant difference between deceased (4 months, SD: 4.75) and surviving patients (5 months, SD: 4. Table 4.

Table 1: Clinical characteristics, treatment, and outcomes of patients with primary gastrointestinal lymphoma.

Case	Age	Sex	Origin	Chief Complaint	Symptom Duration	Patologia	Location	H.pylori	Chemothe Rapy	Surgery	Follow Up Months	DI Sea SE Outcome
1	49	M	Guatemala	UGIB	10 days	DLBCL	C+F	Postive Not	R Chop		1	D
2	86	M	Guatemala	UGIB	14 days	DLBCL	A	Postive Not	R Chop		1	S
3	63	M	Guatemala	AP	3 days	DLBCL	ID	Perfomed	R Chop RDA	IR	5	D
4	66	M	Quetzaltenango	AP	7 days	DLBCL	C	Postive Not	Epoch	IR	2	S
5	57	F	Quetzaltenango	AP	1 week	DLBCL	A	Postive Not	OTROS POLA/B CHOP	PG	4	S
6	60	M	Guatemala	AP	1 week	DLBCL	IM	Perfomed	R CHOP R MNI CHOP		4	S
7	33	M	Suchitepequez	AP	4 days	DLBCL	ID	Postive	CHOP	IR	9	S
8	89	M	Guatemala	UGIB	10 days	DLBCL	A	Postive Not	R CHOP R MNI CHOP		3	S
9	49	M	Guatemala	UGIB	18 days	DLBCL	A	Postive Not	CHOP	PG	12	S
10	31	M	Santa Rosa	AP	2 weeks	DLBCL	IM	Postive Not	ST POLA R		2	M
11	46	M	Guatemala	UGIB	20 days	DLBCL	ID	Perfomed	CHOP		11	M

Abbreviations used: DLBCL = Diffuse large B-cell lymphoma; MALT = Mucosa-associated lymphoid tissue lymphoma; UGIB = Upper gastrointestinal bleeding; AP = Abdominal pain; C = Colon; F = Fundus; A = Antrum; ID = Duodenum; IM = Ileum; IR = Intestinal resection; PG = Partial gastrectomy; ST = Supportive treatment; POLA = Polatuzumab; D= Dead; S = Survival.

Table 2: Comparison between surviving and deceased patients: epidemiological, clinical, and biochemical variables.

VARIABLE	**OVERALL**	**YES**	**DEAD NO**
Age, Mean (SD)	57.18 (18.68)	47.25(13.12)	62.85 (19.81)
Sex, n (%)			
Male	10 (90.9)	4 (100)	6 (85.7)
Female	1 (9.1)	-	1 (14.3)
Clinical Stage, n (%)			
I	1 (9.1)	-	1 (14.3)
> I	10 (90.9)	4 (100)	6 (85.7)
Symptoms, n (%)			
Weight loss	3 (27.3)	1 (25)	3 (42.9)
Vomiting	3 (27.3)	4 (100)	3 (42.9)
Melena	3 (27.3)	1 (25)	2 (28.6)
Anemia	3 (27.3)	1 (25)	2 (28.6)
Perforation	2 (18.2)	2 (50)	
Obstruction	4 (36.4)	2 (50)	2(50)
Epigastralgia	7 (63.6)	3 (75)	4 (57.1)
Dyspepsia	4 (36.4)	2 (50)	4 (57.1)
Biochemistry, Mean (SD)			
Hemoglobin (g/dL)	12.18 (2.59)	11.2 (2.36)	12.74 (2.71)
LDH (U/L)	301.63 (109.47)	316 (129.15)	293.42(106.86)
Albumin (g/dL)	3.39 (2.59)	2.85 (0.62)	1,00

Table 3: Endoscopic characteristics of surviving and deceased patients.

VARIABLE	GLOBAL	DEAD	
		SI	NO
Endoscopic findings f (%)			
Ulcerative type	2 (18.2)	1 (25)	1 (14.3)
Exophytic type	1 (9.1)	--	1 (14.3)
Tumor lesion	2 (18.2)	--	2 (286)
Location f (%)			
Gastric antrum	4 (36.4)	--	4 (57.1)
Gastric body/fundus	1 (9.1)	1 (25)	
Small intestine	3 (27.3)	2 (50)	1 (14.3)
Mid intestine	1 (9.1)	1 (25)	1 (14.3)
Colon	1 (9.1)	--	1 (14.3)
H. pylori			
Positive	5 (45.5)	1 (25)	4 (57.1)
Negative	--	--	--
Not performed	6 (54.5)	3 (75)	3 (75)
Pathology			
DLBCL	10 (90.9)	4 (100)	6 (85.7)
MALT	1 (9.1)		1 (14.3)
CD20	11 (100)	4 (100)	7 (100)
CD3	8 (72.7)	3 (75)	7 (100)
BCL6	10 (90.9)	4 (100)	6 (85.7)
C-MYC	10 (90.9)	4 (100)	6 (85.7)
KI-67 Mean (SD)	57.18 (18.68)	80.75 (12.20)	75.71 (27.75)

Table 4: Medical Treatment in Patients with Gastrointestinal Lymphoma.

VARIABLE	GLOBAL	DEAD	
		SI	NO
Type of Therapy f (%)			
Chemotherapy	5 (45.5)	2 (50)	3 (42.9)
Chemotherapy + Surgery	5 (45.5)	1 (25)	4 (57.1)
Chemotherapy Regimen f (%)			
CHOP	1(9.1)	--	1 (14.3)
R-CHOP	4 (364)	2 (50)	2 (28.6)
POLA-R-CHOP	1 (9.1)	--	1 (14.3)
R-MINI CHOP	1 (9.1)	--	1 (14.3)
POLA-R-BENDA	1 (9.1)	1(25)	1 (14.3)
Surgery f (%)			
Partial Gastrectomy	2 (18.2)	--	2 (28.6)
Intestinal Resection	4 (36.4)	1 (25)	3 (42.9)
Disease Duration Time			
Months	4.9 (3.96)	4 (4.75)	5 (4)

5. Discussion

In this study, a cohort of 11 patients with a diagnosis of primary gastrointestinal lymphoma (PGIL) was collected, excluding cases in which gastrointestinal involvement was due to secondary infiltration from systemic lymphoma. Only patients who presented with gastrointestinal symptoms and whose clinical and endoscopic findings were compatible with primary lymphoma were included. PGIL is a rare entity, making this sample representative considering the two-year collection period. Previous studies with longer follow-up periods have reported similarly small cohorts. For instance, a paediatric case series published in Paediatric Haematology and Oncology included 16 PGIL cases collected between 1972 and 2019. Similarly, a study in Mexico reported 28 cases of MALT lymphoma between 2010 and 2015. Another relevant series covering 2013 to 2021 documented 78 PGIL cases (Blackwell Publishing Ltd., 2006). Additionally, a multicentre retrospective study from 1993 to 2004 reported 157 cases over a longer observation period. These data contextualize the low incidence of PGIL and support the representativeness of our sample collected between January 2023 and January 2025. As shown in Table 1,

upper gastrointestinal bleeding (UGIB) was one of the most common clinical presentations, observed in 54.5% of cases. A representative case (Case No. 1) involved a patient who presented solely with gastrointestinal bleeding, without associated systemic symptoms such as fever, weight loss, or night sweats. Upper endoscopy revealed ulcerative lesions in the gastric mucosa, raising suspicion of neoplastic pathology. The endoscopic biopsy, later analysed by the pathology department, confirmed the diagnosis of PGIL. Figure 1 shows the endoscopic features of the ulcerated lesion, highlighting the critical role of endoscopy in detecting these malignancies Figure 1. These findings align with the literature, where gastrointestinal bleeding is reported as the initial manifestation in up to 30% of PGIL cases. Furthermore, the ulcerative pattern is one of the most frequent endoscopic presentations in such patients, emphasizing the need for an appropriate differential diagnosis with other conditions such as peptic ulcer disease or gastric adenocarcinoma. Another relevant manifestation involves exophytic lesions, as observed in Case No. 2, in which an 84-year-old patient presented with a history of gastrointestinal bleeding. The patient reported a four-month history of abdominal pain and weight loss associated with anaemia, raising suspicion of gastrointestinal haemorrhage and prompting referral to the emergency department. Given the presence of alarm symptoms, an upper gastrointestinal endoscopy was performed, revealing an ulcerated exophytic lesion with poorly defined borders located in the gastric body. Additionally, a stenosis in the antrum was observed, secondary to an exophytic lesion involving the entire anterior and posterior walls. On retroflexion, the mucosa of the incisura and gastric fundus showed an irregular surface, while the cardia fold appeared prominent, completely enclosing the endoscope. Moreover, the pylorus showed stenosis with an irregular surface, deviated to the left, but remained patent. Endoscopic biopsies were taken, and histopathological analysis confirmed the diagnosis of gastrointestinal lymphoma Figure 2. Another key finding in our study is that all upper endoscopies performed tested positive for Helicobacter pylori infection, reinforcing the strong association between this pathogen and the development of primary gastrointestinal lymphoma, particularly MALT lymphoma. This aligns with current literature reporting that over 90% of gastric MALT lymphomas are H. pylori-related, and eradication therapy can induce complete remission in early-stage disease. In our cohort, Case No. 8 involved an 89-year-old male who presented with melena of one day's duration and a history of unintentional weight loss (10 pounds over 3 months). Upper GI endoscopy revealed a 5 cm mass in the greater curvature, with erythematous mucosa, irregular borders, diffuse infiltration, and ulceration involving the lesser curvature and antrum, extending to the prepyloric region. The pylorus was displaced to the left but remained passable with the endoscope. Histopathological examination confirmed a high-grade B-cell lymphoma, consistent with diffuse large B-cell lymphoma (DLBCL), positive for CD20, negative for CD30, and with a Ki-67 proliferation index of 90%. Considering the patient's advanced age and comorbidities, treatment was initiated with R-MINI CHOP, leading to a favourable clinical outcome Figure 3. In our review, we identified a single case of MALT lymphoma in a 49-year-old patient with a history of upper gastrointestinal bleeding, anaemia (Hb 11.5 g/dL), and elevated LDH (450 U/L). Upper endoscopy did not reveal macroscopic tumour lesions in the gastric antrum; however, due to clinical suspicion, targeted biopsies were taken. Histopathological analysis confirmed the diagnosis, showing gastric mucosa infiltrated by a lymphoproliferative process composed of small cells with scant cytoplasm and round nuclei with homogeneous chromatin. Lymphoepithelial lesions were observed in the antral glands, characterized by more than three lymphoid cells infiltrating and destroying the glands. Giemsa stain was strongly positive (+++) for Helicobacter pylori. Immunohistochemistry revealed CD20 positivity, reactive T lymphocytes positive for CD3, negative staining for CD10 and cyclin D1, CD43 partially positive (+/−), and Ki-67 expression of 15%, findings consistent with extranidal marginal zone lymphoma of MALT type. The patient was treated with R-CHOP chemotherapy and underwent partial gastrectomy, with good clinical and surgical response. He has completed six cycles of chemotherapy and remains in favourable clinical follow-up after 12 months Figure 4. Case No. 11 involved a 46-year-old male patient who presented with intestinal obstruction and underwent exploratory laparotomy, which revealed a hypogastric mass measuring 80×65 mm. Histopathological examination confirmed diffuse large B-cell lymphoma (DLBCL) with positive immunohistochemical expression of CD20, CD10, BCL-6, MUM1, BCL-2, and C-MYC (70%). The patient was initially treated with R-CHOP chemotherapy, completing six cycles. However, due to evidence of disease progression, the treatment regimen was changed to Polatuzumab Vedotin, Bendamustine, and Rituximab (Pola-Benda-R). Subsequently, the patient developed surgical complications, including an intestinal fistula, and was re-hospitalized to receive the second cycle of Pola-Benda-R. Despite this, he experienced recurrent symptoms of intestinal obstruction. An emergency surgery revealed intestinal perforation, and the patient died due to postoperative complications Figure 5. Imaging shows evidence of distal small and large bowel obstruction due to impacted fecaloma in the rectum, mesorectum, and sigmoid colon. No extrinsic or intrinsic masses were identified in the upper hemiabdomen to explain the obstruction, suggesting an underlying lymphoproliferative process. This study provides a detailed characterization of patients with primary gastrointestinal lymphoma (PGIL) treated at the Guatemalan Social Security Institute (IGSS), highlighting the heterogeneity in clinical and endoscopic presentations of this disease. Upper gastrointestinal bleeding and abdominal pain were the most common symptoms, consistent with previous studies describing the clinical behaviour of these tumours in other populations. The most frequent site of involvement was the stomach, particularly the gastric antrum, followed by the small intestine, in line with existing literature identifying the stomach as the most commonly affected site in primary gastrointestinal lymphomas. Helicobacter pylori infection was documented in a significant proportion of patients, especially in those with MALT lymphoma, reinforcing the well-established

pathogenic relationship reported in multiple epidemiological studies. Histologically, the majority of cases were diagnosed as diffuse large B-cell lymphoma (DLBCL), also reported as the most frequent and aggressive subtype of PGIL in other case series. The most commonly used chemotherapy regimen was R-CHOP, with some cases requiring adjuvant surgery due to obstructive or severe haemorrhagic complications. The mortality rate was 36.4%, and it was observed that deceased patients had a higher proliferative index (elevated KI-67), more frequent alarm symptoms, and more advanced disease stages at diagnosis. This study emphasizes the importance of early diagnosis through targeted endoscopic biopsies and the need for a multidisciplinary approach to optimize treatment and improve outcomes in this rare but serious condition.

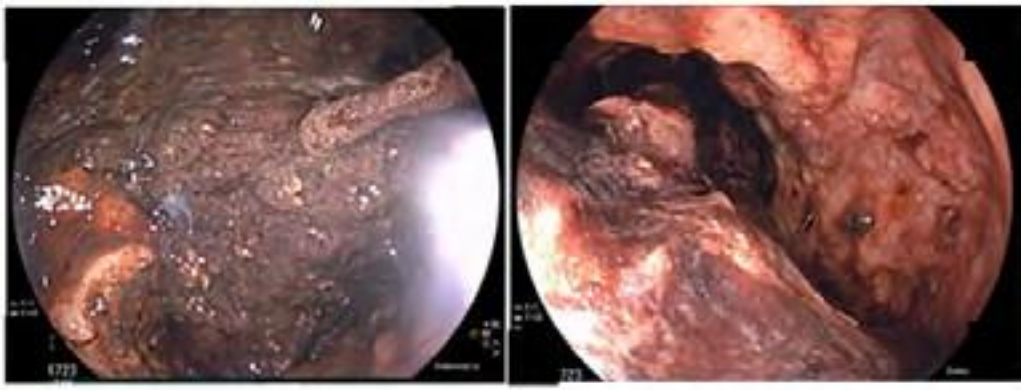

Figure 1: Endoscopy: An ulcerated lesion with raised and infiltrative borders and multiple visible vessels is observed at the level of the gastric body. (Case 01).

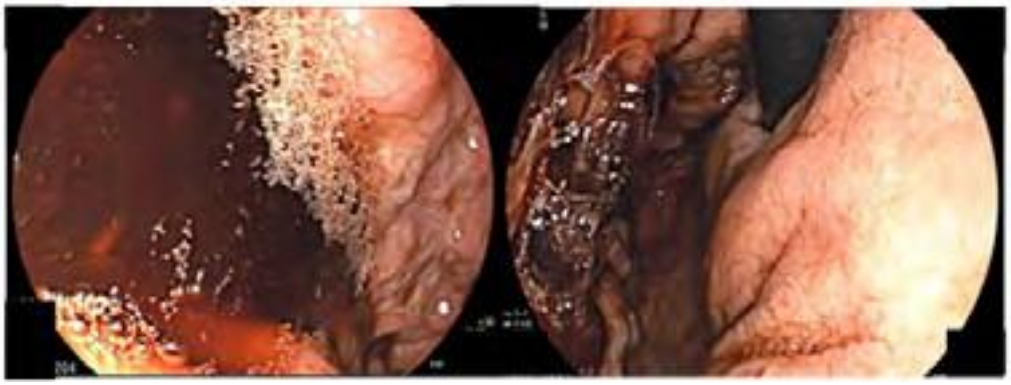

Figure 2: Upper gastrointestinal endoscopy of Case No. 2.

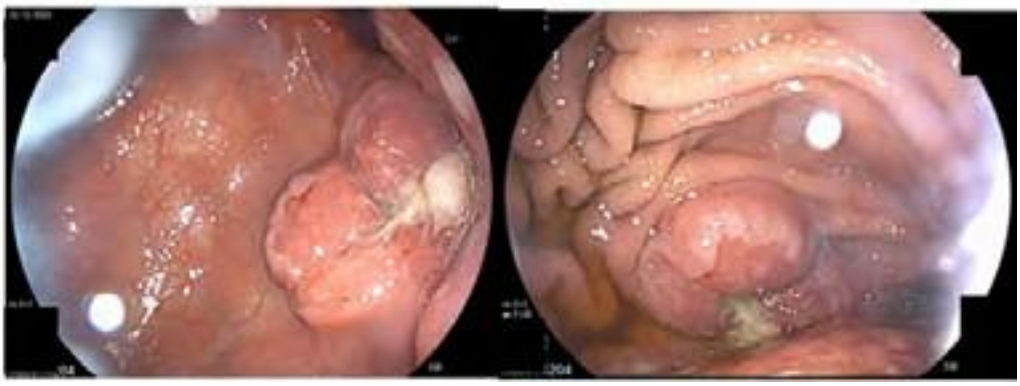

Figure 3: Upper gastrointestinal endoscopy of Case No. 8.

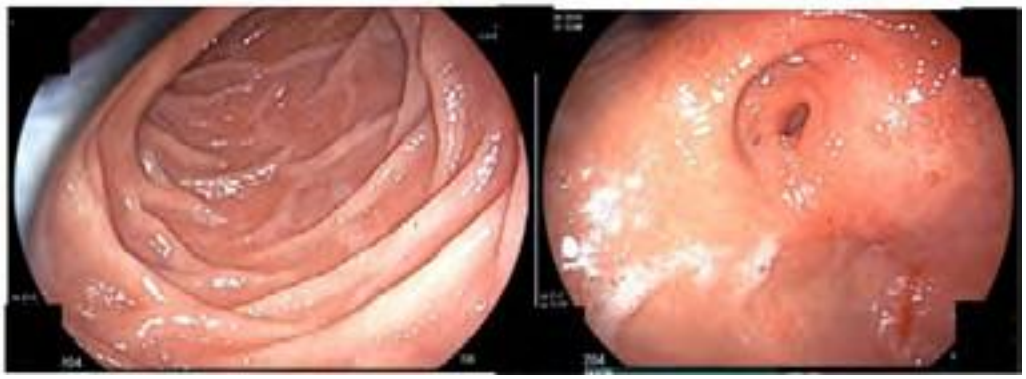

Figure 4: Upper gastrointestinal endoscopy of Case No. 9.

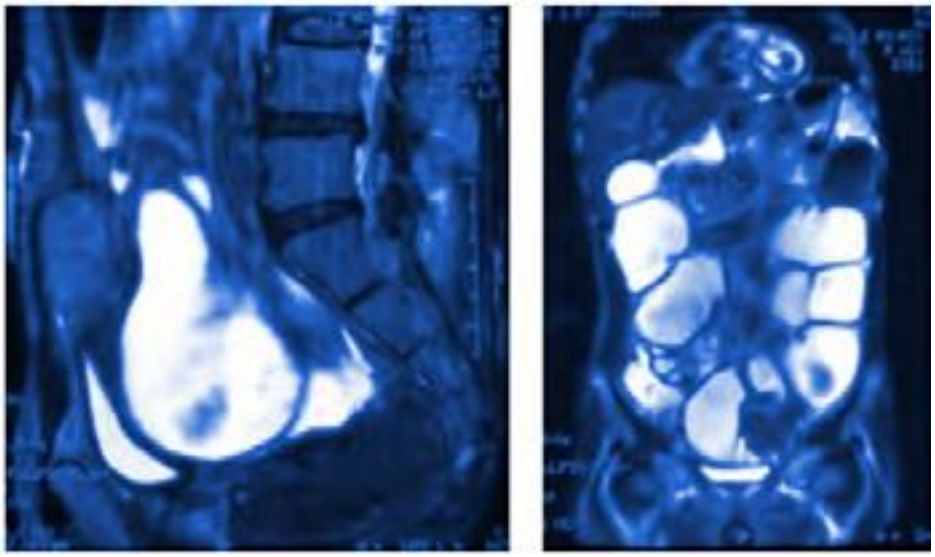

Figure 5: Abdominal MRI – Case No. 11.

6. Conclusions

Primary gastrointestinal lymphoma remains a diagnostic and therapeutic challenge due to its nonspecific clinical presentation and low incidence. Our findings confirm that gastrointestinal bleeding and abdominal pain are key symptoms that should raise suspicion for this pathology in high-risk patients. The most common site of involvement was the stomach, predominantly with the DLBCL subtype, and a significant association with Helicobacter pylori was documented in MALT lymphoma cases. R-CHOP chemotherapy was the most frequently employed treatment regimen. Mortality was more prevalent among patients with advanced disease stages, high KI-67 proliferation index, and severe clinical compromise at diagnosis. This study highlights the need for prospective studies with a larger number of patients to better understand the clinical course and treatment of gastrointestinal lymphoma in our population.

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