

The Histopathological Panorama of Ileocecal Lymphomas: A Disparate Entity Amongst Customary Primary Gastro-Intestinal Lymphoma Stereotypes- A Microscopic Rummage Through a Nexus of 14 Cases

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ABSTRACT

Background: The most common extra-nodal site for non-Hodgkin's lymphoma is the Gastrointestinal tract, with Ileo-cecal being the commonest. Primary Gastrointestinal lymphoma is considered to be rare (1-4 %). We aim to study the histopathological pattern of Primary Gastrointestinal lymphomas (PGIL) in the region of Kashmir.

Material and Methods: This study was done in a tertiary care centre of Kashmir, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar. Jammu & Kashmir over the period from January 2022 to January 2025.

Results: This study includes a total of 14 cases of PGIL with male predominance. Most cases were observed in the 5th to 6th decade of life. Diffuse large B cell lymphoma (10 cases) was most prevalent PGIL, followed by Mantle cell lymphoma (2 cases) and Burkitt's lymphoma (2 cases) each. The ileum was the most common site. Colonoscopic, radiological evaluation, along with immunohistochemical work, was also done.

Keywords: Lymphoma, PGIL, non-Hodgkins lymphomas, Primary gastrointestinal lymphomas, CHOP, MALToma.

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INTRODUCTION

Primary gastrointestinal lymphoma is a rare malignancy, accounting for only 1% to 4% of all gastrointestinal cancers¹. These malignancies originate from the lymphocytes of the gastrointestinal (GI) tract, making the digestive tract the most frequent extranodal site for non-Hodgkin lymphomas². The histological classification of lymphomas has been a longstanding subject of debate among both clinicians and pathologists³. Several risk factors have been implicated in the pathogenesis of gastrointestinal lymphomas, including *Helicobacter pylori* (*H. pylori*) infection, human immunodeficiency virus (HIV), celiac disease, *Campylobacter jejuni* (*C. jejuni*), Epstein-Barr virus (EBV), hepatitis B virus (HBV), human T-cell

lymphotropic virus-1 (HTLV-1), inflammatory bowel disease, and immunosuppression.²

Histopathologically, approximately 90% of primary gastrointestinal lymphomas are of B-cell lineage, with only a small proportion comprising T-cell lymphomas and Hodgkin lymphoma¹. B-cell non-Hodgkin lymphomas dominate this category, with diffuse large B-cell lymphoma (DLBCL) and marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) being the most prevalent types. T-cell lymphomas are relatively uncommon, representing only 4% to 6% of cases. While MALT lymphoma and DLBCL

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typically affect the stomach, mantle cell lymphoma (MCL) is more frequently found in the terminal ileum, jejunum, and colon. Conversely, follicular lymphoma and enteropathy-associated T-cell lymphoma are found in the small intestine². The ileum is the most commonly involved site. The clinical presentation of small intestinal lymphomas is nonspecific, with symptoms such as colicky abdominal pain, nausea, vomiting, weight loss, and, less commonly, acute obstructive symptoms, intussusception, perforation, or diarrhoea. Burkitt's lymphoma, which primarily affects children, is associated with EBV and HIV/AIDS.[1] Radiologic findings for small intestinal lymphoma are often nonspecific, making it challenging to distinguish from

other benign and malignant lesions. Common imaging features seen in barium studies and CT scans include polypoid formations, multiple nodules, infiltrative formations, endo-exocentric formations with excavation and fistulization, and mesenteric invasive patterns characterised by extraluminal masses. Burkitt lymphoma typically presents as a bulky mass in the right lower quadrant¹.

MATERIALS AND METHODS

An observational study was conducted in the Department of Pathology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, between January 2022 and January 2025.

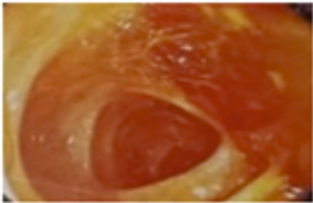
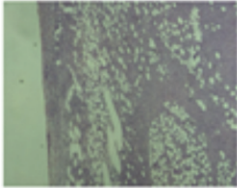
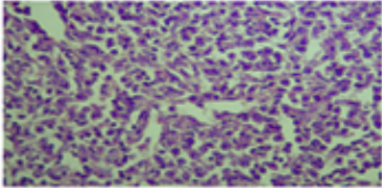
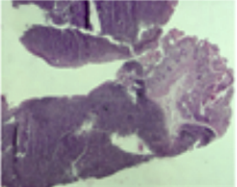
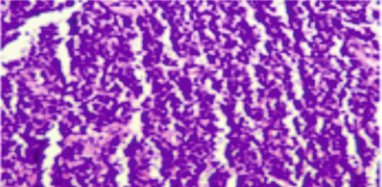
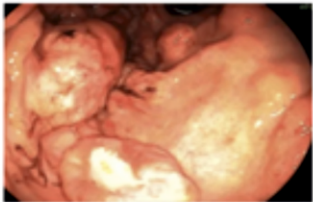
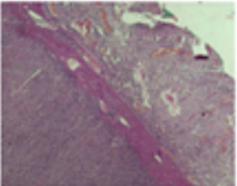
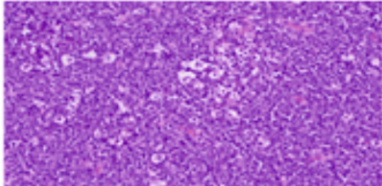
	COLONOSCOPY	HPE	
D L B C L	 Endoscopy revealing a fungating ulcer lesion	 H&E 10x Intestinal wall diffusely infiltrated by sheets of large atypical lymphoid cells reaching into the subserosal fat upto the serosal lining	 H&E 40x Sheets of atypical lymphoid cells in diffuse pattern. Most of the tumor cells resemble centroblasts and immunoblasts
M C L	 Protruding without ulcerative lesions involving the colon	 H&E 10x Mucosal bits revealing ileal lining epithelium with underlying wall showing sheets of monomorphic small lymphoid cells	 H&E 40x Small to medium monomorphic cells with irregular nuclear borders, clumped chromatin, and few hyalinized vessels
B K L	 Numerous elevated lesions, some with central ulceration, a bulge measuring around 3 cm	 H&E 10x Intestinal wall infiltrated by sheets of small lymphoid cells infiltrating upto the muscularis propria	 H&E 40x Sheets of monotonous intermediate-sized cells with "starry sky" appearance and tingible body macrophages

Table 1: Comparison of Colonoscopic and Microscopic features of various lymphoma

RESULTS

Between January 2022 and January 2025, a total of 14 cases of lymphoma were diagnosed in the ileocecal region. The histopathological samples received in our department were ileal resections, right hemicolectomy, ileo-cecal valve and small Colonoscopic biopsies. Of these, diffuse large B-cell lymphoma (DLBCL) was the most prevalent, accounting for 10 cases, followed by 2 cases of mantle cell lymphoma and 2 cases of Burkitt's lymphoma. A strong male predominance was observed, with a male-to-female ratio of 12:2. The majority of cases were diagnosed in patients within the fifth to sixth decades of life, with abdominal pain being the most frequently reported symptom. The ileum was the most commonly affected site, with 8 cases, followed by the caecum (4 cases), while the jejunum and appendix were each involved in 2 cases.

Colonoscopic evaluation revealed characteristic findings, including patchy irregular mucosa, thickened folds, and protruding non-ulcerative lesions, some of which mimicked adenocarcinoma. Histopathological examination of DLBCL cases demonstrated diffuse sheets of atypical lymphoid cells resembling centroblasts and immunoblasts. Immunohistochemistry (IHC) confirmed positivity for CD20, CD10, Kappa, BCL6, and CD79a, with a Ki67 proliferation index of 60–70%. Mantle cell lymphoma, the second most frequently diagnosed lymphoma in this study, was located in the ileum and caecum and exhibited a small to medium monomorphic

population of cells with irregular nuclear borders, clumped chromatin, and occasional hyalinized vessels. IHC analysis showed positivity for CD3, CD20, CD21, CD5, Ki67 (15–18%), cyclin D1, and SOX11, while

markers such as CD10, BCL2, BCL6, CD30, and CD23 were negative. Burkitt's lymphoma, a rare entity in this region, was diagnosed in two pediatric cases involving the appendix. One patient was nine years old, while the other was merely 20 months old, both presenting with acute appendicitis. Following emergency appendectomy, histopathological evaluation of the resected specimens confirmed the diagnosis of Burkitt's lymphoma.

All patients received CHOP or R-CHOP therapy. However, of the 14 patients diagnosed over the past three years, only five survived, indicating a poor prognosis despite treatment. Patients presenting with abdominal pain, fever, gastrointestinal perforation, and bloody stools, particularly when multiple ulcers are detected in the intestinal wall during colonoscopy, should be evaluated for lymphoma to avoid misdiagnosis. Colonoscopy and histopathological analyses play a crucial

Role in determining the tumour type, with DLBCL and mucosa-associated lymphoid tissue (MALT) lymphomas more commonly affecting the stomach and ileum, while mantle cell lymphoma predominantly involves the small intestine and colon.

The standard treatment approach consists of surgical resection followed by chemotherapy. The commonly used regimen includes cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP). Despite aggressive treatment with CHOP and R-CHOP, the prognosis remains poor, with a high mortality rate among the studied cases. The five-year survival rate for non-Hodgkin lymphoma (NHL) varies widely, ranging from 8% to 60%.

Type of Lymphoma	IHC Positive	IHC Negative
DLBCL (10 cases)	CD20,CD10,Kappa ki67(50-60%),BCL6 CD79a	CD3, CD5, Lamda,BCL2,MUM1
Mantle Cell Lymphoma (2 cases)	CD3,CD20,CD21, CD5,Ki67(15-18%), cyclin D1,SOX11	CD10,BCL2, BCL6,CD30, CD23,
Burkitt Lymphoma (2 case)	CD20,PAX5,BCL6, CD10,Ki67(100%)	BCL2,CD3, CD5,CD7

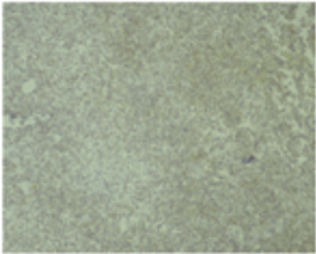
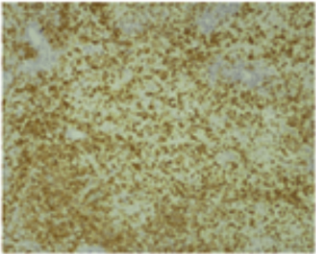
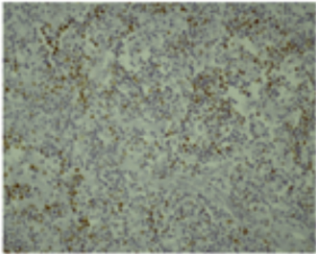
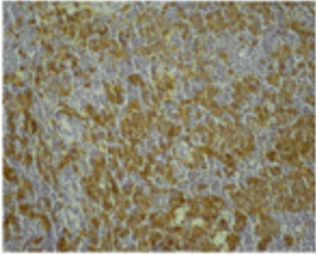
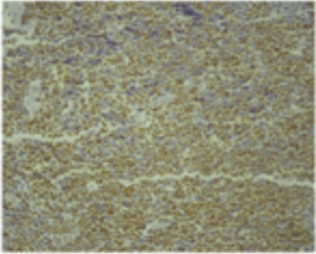
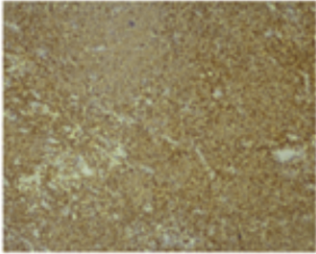
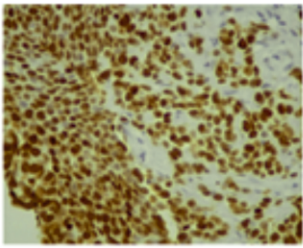
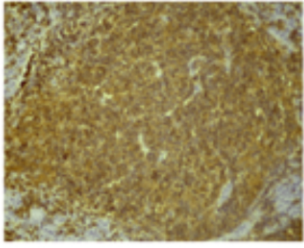
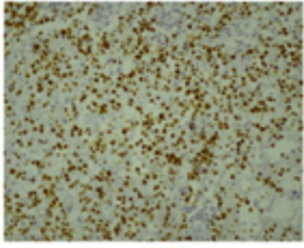
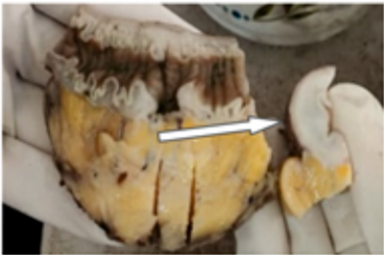
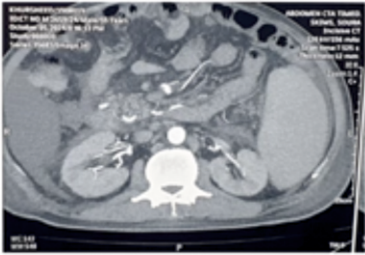
	IHC		
DLBCL			
	CD10 (10X) Positive	CD20 (10X) Positive	BCL6 (20X) (40% Positivity)
MCL			
	CD23 (40X) Positive	Cyclin D1 (40X) Positive	CD 5 (10X) Positive
BKL			
	Ki67 (40X) 100% Positivity	CD20 (20X) Positive	PAX5 (20X) Positive

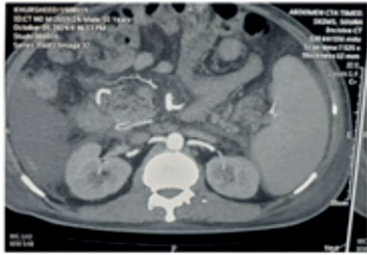
Table 2: Various IHC done for confirmation



Gross image shows a thickened area in the Ileum



CECT Abdomen - Long segment thickening with mural stratification noted in mid ileum - early and late arterial phase enhancement measuring 5.1x5.2 mm



DISCUSSION

The ileocecal valve (IC valve) is a muscular valve which sunders the small intestine from the large intestine, thereby preventing the reflux of colonic contents into the ileum. The IC valve was first documented by the Dutch physician Dr. Nicolaes Tulp, thereby gaining the eponym of Tulp's valve. The characteristic histology of the IC valve shows a change in the mucosal lining with an overt thickening of the muscularis mucosae layer. A thickening of the muscularis propria is also an eminent microscopic feature. There is substantial lymphatic tissue found around this valve⁴. These histomorphological features may make the IC valve more susceptible to the development of lymphomas.

Lymphomas are broadly classified as Hodgkin lymphoma and non-Hodgkin lymphoma. The GI tract is one of the cardinal sites of extra-nodal non-Hodgkin lymphomas, accounting for approximately 30 to 40% of all extra-nodal lymphomas. In a study by Wong MT et. al., most GI lymphomas are non-Hodgkin's mature type B-cell lymphomas, of which MALTomas and diffuse large B-cell lymphomas (DLBCL) are the most frequently occurring histological subtypes⁵. Analogously, in our case series, out of the 14 cases of IC valve lymphomas, DLBCL) was the most prevalent subtype, accounting for 10 cases, followed by 2 cases of Mantle cell lymphoma and 2 cases of Burkitt's lymphoma. The most habitual site of primary GI lymphomas is the stomach, where approximately 75% of Primary GI lymphomas are located. This is followed by the small intestine (8.6%) and subsequently the colon (7%)^{6,7}. Primary colonic lymphomas are rare and comprise about 0.2%-1.2% of all colonic malignancies. Colonic lymphomas are usually located near the ileocecal valve and grow into the terminal ileum⁷. In concordance with this, in our study, the ileum was again the most commonly affected site (8 cases), followed by the caecum (4 cases), while the jejunum and appendix were involved in 2 cases each.

In a study by Mostafa Mosbeh Abdelmaksoud et. al., primary colorectal lymphomas occur mainly in the older age groups between the 5th and 7th decades of life, which was again in coherence with our study but with a starkly

lower male: female ratio of 1.5:¹⁸. Lo Re G et. al. found abdominal pain and weight loss as the most common presenting symptoms. Also, in the study by Bairey O et. al. colonic lymphomas present as abdominal pain (70%), unexplained weight loss (43%) or an abdominal lump (29%) whereas small bowel lymphomas are associated with the frequent symptoms of ileus, P/R bleed, perforation or a palpable mass as the protean symptoms⁹. This again was in harmony with our finding that most patients had abdominal pain as the initial presenting symptom⁷. Abdominal CT scans and barium enemas are the most frequently used imaging tests for diagnosis, although colonoscopy with biopsy is mandatory for a definitive diagnosis⁹. This was supported by our study as well. The exact etiological factors are not known; albeit a few recognised risk factors described for colonic lymphoma are past history of lymphomas, radiotherapy, chemotherapy, immunosuppression, autoimmune diseases and certain viral infections¹⁰.

Different staging systems, such as Ann Arbour, Lugano or the Paris staging system, a modification of the TNM staging system for epithelial tumours, have been used to stage primary GI lymphomas. Some studies have evaluated the efficiency of these three staging systems in predicting clinical outcomes in patients with primary GI lymphomas. The majority of these studies unanimously agreed upon a superiority of the Paris system in predicting overall survival in these patients^{11,15}. Hwang et al demonstrated the relevance of the T parameter in the Paris staging system as a promising prognostic factor in resected intestinal DLBCL¹². However, this prognostic significance has been evidenced only in univariate analysis^{13,14,16}. Therefore, further large-scale studies are needed to substantiate these findings.

The prognosis of localised colonic lymphomas treated with complete surgical resection and superadded chemotherapy has been quoted as efficacious according to the results of many studies¹⁴. The standard regimen includes cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP). Despite aggressive treatment with CHOP and R-CHOP, the five-year survival rate for non-Hodgkin lymphoma still dwindles between 8% to 60%. This strongly implicates the need for additional

research and analysis on this subject.

CONCLUSION

Ileocecal lymphomas, thus, remain an enigmatic clinical entity within the diapason of GI lymphomas. Despite the advancement in various diagnostic modalities, the nonspecific symptoms often lead to a delay in diagnosis. This case series further underscores the paramount importance of histopathological examination and immunohistochemistry in establishing an early and precise diagnosis. While imaging modalities such as CT and PET scans are of incontestable value in the disease staging, a definitive diagnosis still hinges upon a meticulous microscopic evaluation.

Conflict of Interest: None

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Written informed Consent: Taken

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