

Gastrointestinal Lymphoma-Pathological Insights into Morphology and Immunohistochemistry

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Abstract:

Background: Primary gastrointestinal tract lymphoma (PGIL) represents a rare malignancy of GIT accounting for 1-4% of total malignancies. While the gastrointestinal tract is more commonly involved secondarily from nodal lymphoma, primary cases can originate from any part of gastrointestinal tract extending from oropharynx to anal canal. Histopathological examination of biopsy samples taken during endoscopy is the gold standard for diagnosis. PGIL represents a heterogeneous group of malignant neoplasm which differs in terms of etiological factors, pathogenesis, immunohistochemical profile, treatment strategies and prognosis. The present study aimed to evaluate histological subtypes of primary gastrointestinal lymphoma on the basis of morphology, immunohistochemistry and its anatomic distribution.

Materials and Methods: A total of 10 cases of GI lymphomas received during study period of one year were archived and evaluated retrospectively. Proper IHC panel was put for all the cases for categorization of the tumor.

Observations & Results: In this case series, most of the patients were male with only 2 females diagnosed with lymphoma. Patient's age ranged from 3 years to 74 years with caecum being the most commonly affected site with involvement in 4 patients followed by stomach in 3 patients. Histologically, DLBCL was the most common type of lymphoma in this study and was diagnosed in 6 patients; all of these cases were of the germinal center B cell (GCB) subtype. Single case of Burkitt's lymphoma was diagnosed in a three-year-old child.

Conclusion: In recent years, the incidence of lymphoma is rising in young adults, so it is important to diagnose these lesions early. Most of the gastrointestinal lymphomas are indolent and slow growing and have good prognosis if detected early.

Keywords: Primary Gastrointestinal Lymphoma, Histopathological Examination, Immunohistochemical Profile.

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Introduction

Primary gastrointestinal tract lymphoma (PGIL) includes lymphoma that arises from any part of gastrointestinal tract from oropharynx to anal canal. [1] It is a rare malignancy of GIT accounting for 1-4% of total malignancies occurring at this site. [2] However, PGIL is the most common type of extranodal lymphomas accounting for 25-40% of extranodal lymphomas. [1] Gastrointestinal tract (GIT) is more frequently involved secondarily from nodal lymphoma. [3] The incidence of these neoplasms has been increasing in recent years. [4] Stomach is the most common site for GI lymphomas followed by small bowel and colorectum. Esophageal lymphomas are very rare. [5] Stomach accounts for 55%-65% cases of total GI lymphomas. [4] GI lymphomas are slightly

more common in males and commonly present in the sixth decade of life. These patients present with non-specific symptoms such as dyspepsia, bloating, abdominal pain, nausea, GI bleeding, diarrhea, vomiting, weight loss or bowel obstruction. [6] PGIL is mostly Non-Hodgkin's lymphoma. Hodgkin's lymphoma is very rare. B-cell lymphomas are more common in GIT accounting for 80% of total cases and they are more responsive to chemotherapy. [7] The key to definite diagnosis is appropriately directed endoscopic evaluation with biopsies. [6] Primary gastrointestinal lymphoma is defined by Dawson's criteria. It includes (1) Absence of peripheral lymphadenopathy at the time of presentation, (2) Lack of enlarged mediastinal lymph nodes, (3)

Normal total and differential white blood cell count, (4) Predominance of bowel lesion at laparotomy with involvement of lymph nodes only in immediate vicinity (LN which drain the area of primary tumour site), (5) No involvement of spleen and liver. [1]

Aims and Objectives: To study the histological subtypes of primary gastrointestinal lymphoma received in our department during past 1 year on the basis of morphology, immunohistochemistry and its anatomic distribution.

Materials and Methods: After obtaining ethical approval, 10 cases which were reported as GI lymphomas in last 1 year were included in the study. Proper IHC panel was put for all the cases for categorization of the tumour.

Observations and Results:

In this case series, most of the patients were male. Only 2 female patients were diagnosed with lymphoma. Minimum age of patient included in this study was 3 years and maximum age was 74 years. Caecum was the most common site involved with involvement in 4 patients. The second most common affected site was stomach in 3 patients.

Histologically, DLBCL was the most common type of lymphoma in this study. DLBCL was diagnosed in 6 patients. All cases of DLBCL were Germinal Centre B cell (GCB) subtype. Only one child of 3 years was diagnosed with Burkitt's lymphoma.

Table 1: Gross and Immunohistochemistry findings

S.No	Age	Sex	Site of tumour	Gross	IHC		Impression
					Positive markers	Negative IHC markers	
1.	28yrs	Male	Ileo-caecum	Tan white fleshy tumour measuring 10X6X3cm	LCA, CD20, BCL2, BCL6, c-MYC, Ki67 (60%)	CD3, CD10, TdT&MUM1	DLBCL, NOS, GCB subtype
2.	26yrs	Male	Caecum	Tan white tumour measuring 7.5X6X5 cm	LCA, CD20, BCL2, BCL6, c-MYC, Ki67 (90%).	CD3, CD10, TdT&MUM1	DLBCL, NOS, GCB subtype
3.	4yrs	Male	Small intestine	Part of gut in fragmented tissue piece, largest measuring 5X2 cm.	LCA, BCL2, CD10, Ki67 (70%)	EMA, MUM1, TdT	DLBCL, NOS, GCB subtype
4.	35yrs	Male	Caecum	Grey white tumour measuring 3.5X3X2 cm	LCA, CD10, PAX5, BCL6, Ki67 (80%).	EMA, CD 20 MUM1, TdT	DLBCL, NOS, GCB subtype
5.	43yrs	Male	Gastric Ulcer	Multiple grey white soft tissue piece with total volume amounting to 2cc	Diffusely positive for CD 20, Bcl2. CD 23 (positive in residual follicular dendritic cell meshwork), Ki 67 (approx 20% in highest proliferating area)	CD 3, CD 10, Cyclin D1, Mum 1, BCL6, CD 43.	MALT Lymphoma
6.	3yrs	Female	Ileum	Grey white fleshy tumour measuring 8X6X5 cm	CD 10, CD20, BCL6, CMYC, Ki67 (Approx 100%)	TdT, CD 3, BCL2, EBV	Burkitt lymphoma
7.	42yrs	Female	Caecum	Grey white tumour measuring 3.5X3X2 cm	LCA, CD10, PAX5, BCL6, Ki67 (80%).	EMA, CD20 MUM1, TdT	DLBCL, NOS, GCB type
8.	29 yrs	Male	Stomach	3 grey white tissue piece altogether measuring 1	LCA, CD10, PAX5, BCL6, Ki67 (80%).	EMA, CD20 MUM1, TdT	DLBCL, NOS, GCB type

				X0.5X0.2 cm				
9.	74yrs	Male	Stomach	Multiple fragmented grey white tissue bits altogether measuring 1X1X0.5cm	CD20, CD21, CD23(Residual follicular dendritic meshwork), BCL2, Ki67 (20% in highest proliferating area)	CD3, CD10, Cyclin D1, CD43,	Mum1, Bcl6, D1,	MALT Lymphoma
10.	15yrs	Male	Ileum	Grey white tumour measuring 3.5X3X2 cm	CD10, CD20, BCL2, Ki67(15% in highest proliferating area)	CK, D1,CD23, BCL6, SOX11,CMYC	Cyclin D1,	Low grade B cell lymphoma

Figures:

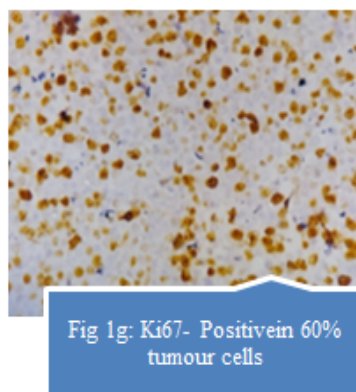
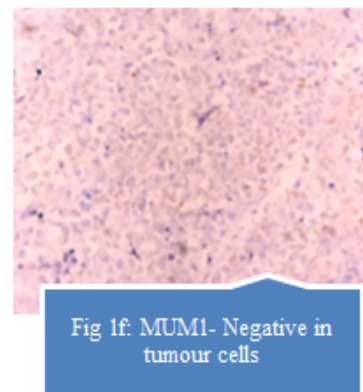
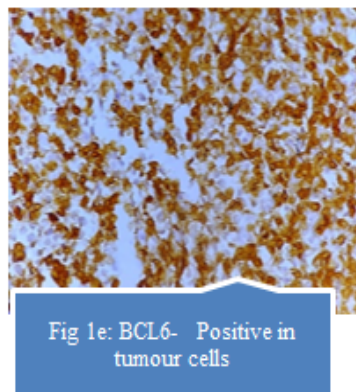
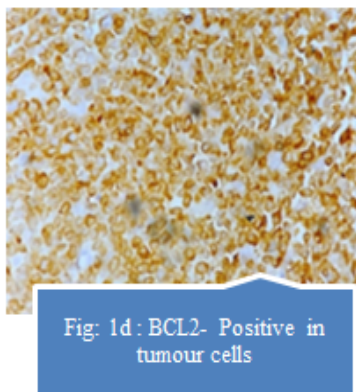
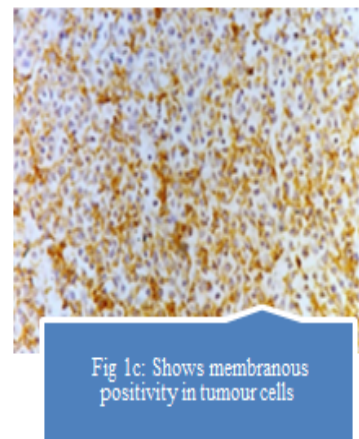
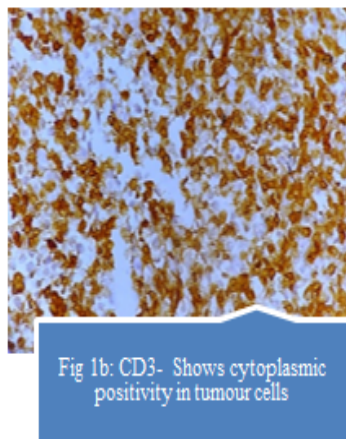
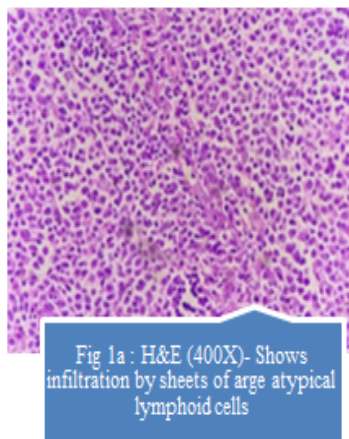
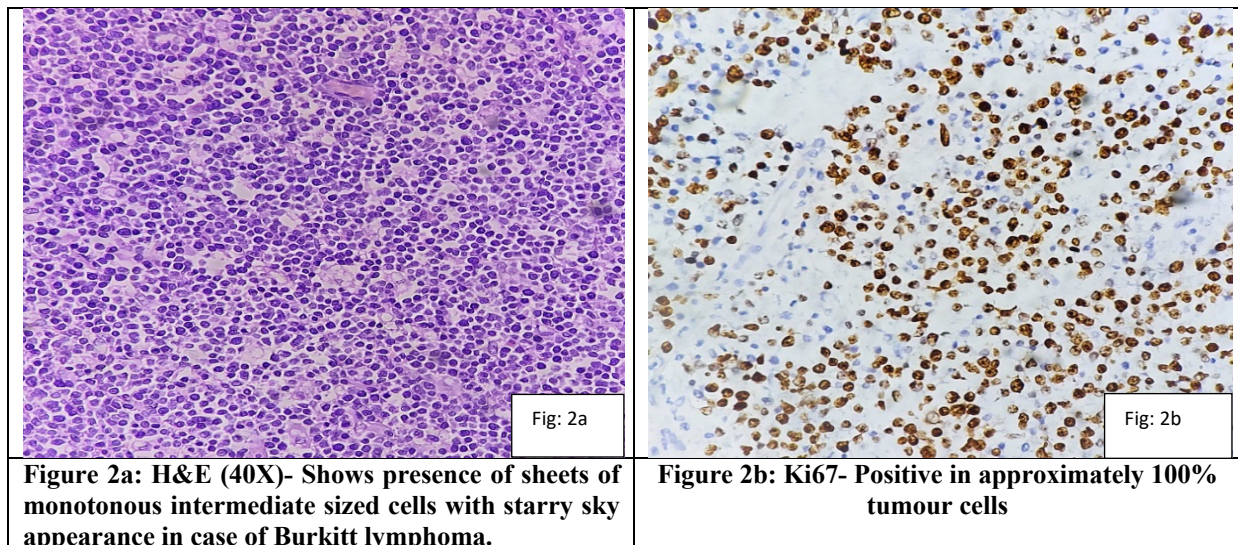


Figure 1: 28 years male presenting with mass in Ileocecal region. On H&E and IHC findings are consistent with DLBCL, NOS, GCB type



Discussion

Endoscopy is first diagnostic modality for visualization of lesion and for obtaining biopsy samples. However, the histopathological examination of biopsy samples taken during endoscopy is the gold standard for diagnosis. [1] Multiple biopsies should be obtained from stomach, gastro-esophageal junction, duodenum since sometimes gastrointestinal lymphoma occurs multifocally. MALT lymphoma and follicular lymphoma most commonly tend to be multifocal. [3]. Many inflammatory and reactive conditions occurring in GIT can mimic and mask lymphoma. [1]

In the previous studies, stomach was the most commonly involved site in GIT followed by small bowel, ileocaecal region and rectum. [9] In stomach, antrum is the most common site involved. The incidence of gastric carcinoma has reduced in previous years but the incidence of primary gastric lymphoma is rising. Primary gastric lymphoma more commonly occurs in patients older than 50 years but can also occur in second decade. DLBCL is the most common histological subtype followed by MALT lymphoma. Chronic gastritis occurring secondary to H. Pylori infection is the most common predisposing factor for MALT lymphoma. [4]

In small intestine, ileum (60-65%) is the most commonly involved site followed by jejunum (20-25%). [10] DLBCL and MALT lymphoma are the most common type of small intestinal lymphoma. [11]

Primary colorectal lymphoma is very rare. Most colorectal lymphomas are secondary due to presence of widespread disease. Caecum, ascending colon and rectum are more often

affected. [8] It most commonly affects males in fifth to seventh decade of life. Primary colorectal lymphoma comprises of low grade B cell lymphoma arising from MALT lymphoma, Marginal cell lymphoma and T cell lymphoma along with large B cell lymphoma. Endoscopically, this neoplasm can present as solid lesion with ulceration mimicking colorectal carcinoma or as polyposis (lymphomatous polyposis). [9]

Ramiz Bayramov and Ramila Abdullayeva conducted a study in 2022 and observed that stomach was the most common site of primary gastrointestinal tract lymphomas. DLBCL was the most common histological subtype at all sites in gastrointestinal tract. [1]

Yu Xiang and Lidi Yao in a study conducted in 2022 observed that stomach was the most commonly involved site followed by small intestine, ileocaecal region, rectum and colon. They also observed that DLBCL was the most common histological subtype accounting for 80% cases. [10]

In a study by Jessica Alvarez-Lesmes et al. in 2021 stomach was the most commonly involved site followed by small intestine, colon and esophagus. They also observed that B cell lymphomas were most common type of Non- Hodgkin lymphoma with DLBCL and MALT lymphomas accounting for majority of cases. [9] In small intestine, ileum (60%-65%) is the most commonly involved site followed by jejunum (20%-25%). DLBCL and MALT lymphoma are most common type of small intestinal lymphoma. [9]

Overall, DLBCL is the most common histological subtype of lymphoma at all sites of GIT. [1] In this study also, DLBCL was the most common histological subtype.

Some forms of lymphoma tend to occur in younger groups. In previous studies it was observed that the incidence of MALT lymphoma increased significantly in patients older than 40 years. [11] In this study also, both patients of MALT lymphoma were above 40 years.

Conclusion

In recent years, the incidence of lymphoma is rising in young adults so it is important to diagnose these lesions early. Though diagnosis of PGIL poses unique challenges, advances in imaging and biopsy techniques have improved diagnostic accuracy. Most of the gastrointestinal lymphomas are indolent and slow growing and have good prognosis if detected early. Prognosis worsens with progression of disease

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