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Clinicopathological Presentation of Primary Non-Epithelial Gastrointestinal Tumors: A Retrospective Study from a Tertiary Care Cancer Hospital

Sasmita Panda [1], Snigdha Rani Nahak [2], Mamita Nayak [2], Debasmita Mahanta [3], Sashibhusan Dash *[4]

[1]Associate Professor Pathology, Department of Pathology, AH Postgraduate Institute of Cancer, Cuttack, Odisha, India.
[2]Assistant Professor, Department of Pathology, A H Postgraduate Institute of Cancer, Cuttack, Odisha, India.
[3]Post Graduate Student, Department of Pathology, A H Postgraduate Institute of Cancer, Cuttack, Odisha, India.
[4]Scientist C, Multidisciplinary Research Unit, PRM Medical College and Hospital, Baripada, Odisha, India.

*Corresponding Author: Sashibhusan Dash; *sashibiotech@gmail.com*

Abstract

Background: Non-epithelial gastrointestinal (GI) tumors are rare, heterogeneous neoplasms of mesenchymal, lymphoid/hematopoietic, or neuroendocrine origin. Limited comprehensive data hinder early diagnosis and optimal management. ***Methods:*** A five-year retrospective study was conducted at a tertiary care cancer hodpital, included histopathologically confirmed primary non-epithelial GI tumors; epithelial tumors were excluded. Demographic, clinical, anatomical, morphological, and immunohistochemical data were reviewed. ***Results:*** Of 66 patients, gastrointestinal stromal tumor (GIST) was most common (34.8%), followed by primary GI melanoma (30.3%) and non-Hodgkin lymphoma (NHL) (27.2%). Rare types included liposarcoma, malignant peripheral nerve sheath tumor, plasmacytoma, ganglioneuroma, and lipoma (each 1.51%). Most patients were 41–60 years old (57.5%); males predominated (M:F = 39:27), especially in melanoma and NHL. The anorectum (36.3%) was the most frequent site, mainly due to melanoma, followed by the stomach (30.3%) and small intestine. GISTs occurred more often in the small intestine than the stomach, opposite to global trends. Histopathology and immunohistochemistry were essential for accurate diagnosis, especially for rare tumors. ***Conclusions:*** GIST, melanoma, and NHL predominate among non-epithelial GI tumors, mainly affecting middle-aged to elderly adults. The high frequency of anorectal melanoma and small-intestinal GIST suggests regional or referral influences and underscores the need for thorough small bowel evaluation. Rare tumors require meticulous pathological workup to avoid misdiagnosis. Multicenter and molecular studies are needed to refine epidemiologic understanding and improve outcomes.

Keywords: ***Gastrointestinal stromal tumor, primary gastrointestinal melanoma, gastrointestinal lymphoma, non-epithelial tumors, clinicopathology.***

Introduction

The gastrointestinal tract (GIT) is a hollow organ lined by a mucous membrane. Most tumors of the GIT are of epithelial origin; however, non-epithelial tumors of the gastrointestinal (GI) tract form a rare and heterogeneous group of neoplasms that originate from mesenchymal, neuroendocrine, or lymphoid/hematopoietic cells. There is a wide range of malignant tumors within this group [1]. Malignant tumors include mesenchymal tumors such as gastrointestinal stromal tumors (GISTs), leiomyomas, and leiomyosarcomas, as well as schwannomas, neuroendocrine tumors (NETs), and lymphomas [2-5].

Diagnosis of non-epithelial GI tumors is challenging. Imaging and endoscopy often reveal submucosal masses, but definitive identification relies on histopathology and immunohistochemistry [2]. Misdiagnosis can delay appropriate therapy, underscoring the need for accurate classification [1].

Despite extensive knowledge about individual tumor types, integrative clinicopathological studies covering the entire spectrum of non-epithelial GI tumors are scarce. This gap hinders early recognition and optimal management, highlighting the importance of comprehensive studies to unify epidemiological, morphological, immunophenotypic, and clinical data for these rare but significant malignancies. In this study, we aim to determine the incidence and clinicopathological presentation of non-epithelial tumors of the GI tract.

Materials and Methods

This hospital based retrospective observational study conducted on patients histopathologically diagnosed with primary non-epithelial tumors of the gastrointestinal (GI) tract in a tertiary care cancer hospital last five years. Patients diagnosed histopathologically with epithelial tumors were excluded from the study.

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Data collected for all non-epithelial tumors included patient age, sex, tumor site, gross features, histomorphological characteristics, and immunohistochemical profiles. Presenting signs and symptoms were also documented. The study was approved by the institutional ethics committee.

Statistical analysis

The collected continuous data were represented as mean and standard deviation or median. Categorical data were represented as frequency and percentage.

Result

In this cohort, the most common primary non-epithelial gastrointestinal tract tumor was gastrointestinal stromal tumor (GIST) (34.8%), followed by melanoma (30.3%) and non-Hodgkin lymphoma (NHL) (27.2%). Rare tumor types included liposarcoma, malignant peripheral nerve sheath tumor (MPNST), plasmacytoma, ganglioneuroma, and lipoma, each accounting for 1.51% of cases. The majority of patients (57.5%) were in the 41–60-year age group, with an additional 25.75% above 61 years, indicating a clear middle-aged to elderly predominance; younger patients (<20 years) represented only 3.03% of cases. Overall, there was a male predominance (M: F = 39:27), with melanoma and NHL showing a clear male bias, whereas liposarcoma, MPNST, plasmacytoma, ganglioneuroma, and lipoma were seen exclusively in females in this series. The anorectum was the most common tumor site (36.3%), largely driven by melanoma cases, followed by the stomach (30.3%), which was primarily associated with NHL and GIST. Other sites, such as the small intestine (duodenum, jejunum, ileum), ascending colon, cecum, pancreas, and gastroesophageal junction, were less frequently involved. Overall, GIST, melanoma, and NHL emerged as the predominant non-epithelial GI tract tumors in this study, most often affecting middle-aged to older adults, with a slight male predominance and a tendency to localize to the anorectum and stomach (**Table 1**).

Table 1: Demographic and site distribution of primary non-epithelial gastrointestinal tumors.

Parameters	GIST	Melanoma	NHL	Liposarcoma	MPNST	Plasmacytoma	Ganglioneuroma	Lipoma	Total (%)
<20	-	-	1	-	-	1	-	-	2 (3.03)
21-40	5	2	2	-	-	-	-	-	9 (13.63)
41-60	12	10	13	1	1	-	1	-	38 (57.5)
>61	6	8	2	-	-	-	-	1	17(25.75)
Mean age									
Male:Female	1:1.3	2.3:1	2:1	0:1	0:1	1:0	1:0	1:0	39:27
GE junction	-	-	1	-	-	-	-	-	1 (1.51)
Stomach	7	1	11	-	-	1	-	-	20 (30.3)
Pancreas	1	-	-	-	-	-	-	-	1 (1.51)
Duodenum	3	-	-	-	-	-	-	-	1 (1.51)
Jejunum	5	-	1	-	-	-	-	-	4 (6.06)
Ileum	4	-	1	1	-	-	-	-	3 (4.54)
Ascending Colon	1	-	2	-	-	-	1	-	4 (6.06)
Cecum	1	-	-	-	-	-	-	-	1 (1.51)
Anorectum	1	19	2	-	1	-	-	1	24 (36.3)
Total (%)	23(34.8)	20 (30.3)	18 (27.2)	1(1.51)	1 (1.51)	1 (1.51)	1 (1.51)	1 (1.51)	66 (100)

Clinicopathological presentation of non-epithelial GIT tumors

Gastrointestinal stromal tumors (GISTs)

The mean age at diagnosis was 49.08 ± 14.73 years, with a range of 21–70 years. The male-to-female ratio was 1:1.3. The most common site was the small intestine (n = 12), followed by the stomach (n = 8). We also encountered a rare gastrointestinal stromal tumor arising from the head of the pancreas. The median tumor size was 7.0 cm (range: 3.9–27 cm). Regarding histomorphology, 14 cases (60.86%) were of the spindle cell type, 5 cases (21.73%) were epithelioid cell type, and 4 cases (17.39%) were pleomorphic type. A mitotic rate of >10/50 high-power fields (HPF) was observed in 51% of cases. Among the 23 patients, 18 underwent curative surgery, while 5 had unresectable disease and received only palliative therapy.

Malignant melanoma

Over the study period, 20 cases of primary gastrointestinal tract (GIT) melanoma were identified, including three cases of amelanotic malignant melanoma of the anorectum. Most patients presented with right-sided abdominal pain, discomfort, nausea, and weight loss. Histomorphology combined with immunohistochemical markers (S100, HMB45, and Melan-A) confirmed the diagnosis.

Non-Hodgkin Lymphoma (NHL)

Primary GIT lymphomas totaled 18 cases, with diffuse large B-cell lymphoma (DLBCL) being the most common subtype (15 cases; 83.3%), followed by low-grade marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) type (3 cases; 16.6%). The stomach was the most frequent site (11 cases; 61.1%). Several uncommon types of GIT lymphoma were also observed (**Table 1**). Four patients underwent surgical resection. All cases were diagnosed and categorized using histomorphology and immunohistochemistry.

Liposarcoma

A 45-year-old female presented with abdominal pain, vomiting, and constipation. Physical examination revealed epigastric tenderness without a palpable mass. Laboratory investigations and tumor markers were within normal limits. CT imaging revealed a mass in the ileum. Wide local resection of the affected small bowel segment was performed. Histopathology revealed adipose tissue of varying sizes with atypical cells. Immunohistochemistry confirmed the

diagnosis of primary small bowel liposarcoma.The patient was discharged on postoperative day 11 without complications.

Malignant Peripheral Nerve Sheath Tumor (MPNST)

A 47-year-old female presented with abdominal pain and diarrhea. Colonoscopy and CT scan revealed a polypoidal anal canal mass. Wide local excision was performed. Histomorphology and S100 positivity confirmed MPNST of the anal canal. The patient was referred to medical and radiation oncology for further management.

Plasmacytoma

An 11-year-old boy presented with malaena and loss of appetite. Examination revealed pallor, and hemoglobin was 9 g/dL. Biochemistry was normal. CT scan revealed a 9.6 × 12.2 cm lesion from the greater curvature of the stomach. Partial gastrectomy was performed. Histopathology showed sheets of medium-sized cells with eosinophilic cytoplasm and eccentric nuclei; the overlying mucosa was unremarkable. No features of chronic gastritis or H. pylori infection were noted. Further workup ruled out multiple myeloma, fulfilling criteria for primary gastric plasmacytoma (PGP).

Ganglioneuroma

A 42-year-old male with chronic constipation, hypertension, type 2 diabetes, and GERD underwent screening colonoscopy. A non-bleeding 8 mm polyp was found in the ascending colon and removed via excisional polypectomy. Histopathology showed proliferation of stromal and ganglion cells in the lamina propria.

Lipoma

A 70-year-old male presented with chronic constipation and a prolapsed anorectal mass, along with anal pain and bleeding per rectum. There was no history of hemorrhoids or prolapse. Physical examination revealed a firm, well-circumscribed, tender, hyperemic mass. Abdominal exam was unremarkable. Preoperative labs were normal. Digital rectal examination was performed, and the mass was excised. Histopathology revealed intact colonic mucosa with circumscribed submucosal adipose tissue. The postoperative course was uneventful.

Discussion and Conclusion

Our case series demonstrated that gastrointestinal stromal tumors (GISTs), primary gastrointestinal (GI) melanomas, and non-Hodgkin lymphomas (NHL) were the predominant nonepithelial GI tumors, accounting for 34.8%, 30.3%, and 27.2% of cases, respectively. GISTs, the most common mesenchymal tumors of the GI tract, [6] occurred more frequently in the small intestine (52%) than the stomach (35%) in our series, contrasting with population data showing gastric predominance [7]. Histologically, they comprised 60.9% spindle-cell, 21.7% epithelioid, and 17.4% pleomorphic subtypes, aligning with published patterns,[7,8] though our cohort was slightly younger and more often female than typically reported [9].

Primary GI melanomas, despite their extreme rarity (incidence ~0.36/million), were the second most common a predilection for the anorectal region [10]. Our 20 cases (including 3 amelanotic anorectal melanomas) underscore this: the anorectum was the single most common tumor site in the cohort (driven by melanomas). This matches SEER data showing the highest PGIM incidence in the anorectum and large bowel. Most literature notes a female predominance and advanced age (>70 years) for mucosal melanomas [11]. In contrast, our melanomas occurred in a relatively younger, male-predominant group. All cases were confirmed by standard melanocytic markers (S100, HMB45, Melan-A). Overall, our melanoma findings are consistent with case series emphasizing the rarity and aggressive nature of anorectal melanoma [10,11]. while highlighting variation in demographics.

Primary GI NHL most often involves the stomach (60-75% of cases) [5]. Our data reflect this: 61% of lymphomas arose in the stomach, and the remainder in intestine or colon. Histologically, diffuse large B-cell lymphoma was the dominant subtype (83%), with marginal-zone (MALT) lymphoma comprising the rest. This echoes known patterns: DLBCL is the most common GI lymphoma, followed by MALT [12]. MALT lymphomas are often linked to H. pylori, which was not explicitly studied here, but is likely relevant in some cases. Overall, the clinicopathologic profile of our GI lymphomas agrees with previous reports,[12] reinforcing that gastric DLBCL/MALT variants are the typical nonepithelial gastric malignancies.

We encountered several exceptionally uncommon GI neoplasms. Primary GI liposarcoma is extremely rare – one series described only 8 cases in decades [13]. In that series most patients were older (median ~68.5 years), whereas our patient was unusually young (45 years). As in literature, the tumor originated in the ileum submucosa and required wide excision; careful distinction from GIST on histology (e.g. MDM2/CDK4 IHC) was critical as reported [13]. Malignant peripheral nerve sheath tumors of the GI tract are likewise very rare and aggressive. Published reports of anorectal MPNSTs come only as isolated case studies [14]. Consistent with that, our anal-canal MPNST (S100-positive) was diagnosed after ruling out more common entities. Primary gastric plasmacytomas account for only about 2% of extramedullary plasmacytomas [15]. Our 11-year-old's gastric lesion (work-up excluded myeloma) fits the criteria of solitary plasmacytoma. GI ganglioneuromas are benign neural tumors of neural-crest origin and occur sporadically or in syndromes [16]. We found an isolated colonic polypoid ganglioneuroma, aligning with reports that solitary polypoid ganglioneuroma is incidental and asymptomatic. Unlike the above, GI lipomas are relatively common benign lesions - the colon is the most frequent site (65-75% of GI lipomas) and colonic lipomas are the second most common benign colonic tumor [17]. Our anorectal lipoma case (large, prolapsing) is typical of symptomatic submucosal lipomas.

This case series on non-epithelial gastrointestinal tract (GIT) tumors offers crucial clinical insights despite its descriptive nature. It emphasizes the need for clinicians to broaden differential diagnoses for GI symptoms, considering rare non-epithelial tumors like liposarcoma, MPNST, plasmacytoma, ganglioneuroma, and lipoma, which often present with non-specific symptoms. The study highlights that gastrointestinal stromal tumors (GIST), melanoma, and non-Hodgkin lymphoma (NHL) are the predominant non-epithelial tumors, typically affecting middle-aged to elderly males, with common sites being the anorectum (melanoma) and stomach (NHL and GIST).

Specific implications include recognizing GIST's varied sites and the importance of histomorphology and mitotic rate for prognosis, as well as the critical role of immunohistochemistry (S100, HMB45, Melan-A) in diagnosing often amelanotic primary GI melanoma. For NHL, the prevalence of DLBCL and MALT lymphoma, often in the stomach, is noted. The detailed descriptions of rare tumors like liposarcoma and plasmacytoma provide examples of their varied presentations, including a rare pediatric case of plasmacytoma, and the potential for incidental findings like ganglioneuroma.

Overall, the series underscores the necessity of a comprehensive diagnostic approach involving clinical assessment, imaging, and especially detailed histopathology with immunohistochemistry, which remains the gold standard for definitive diagnosis and classification of these often-challenging tumors. While limited by its case series design (generalizability, selection bias, lack of control group, and small numbers for rare tumors), the study serves as a valuable educational resource, enhancing awareness and guiding diagnostic strategies for these uncommon but significant GI malignancies.

Future research should investigate the molecular and genetic profiles of these tumors across diverse populations to better understand regional variations in site distribution, age, and sex predilections. Larger multicenter studies are warranted to determine whether the male predominance observed for melanoma and NHL in this cohort represents a true epidemiological trend or a sampling artifact. Prospective studies are also needed to evaluate long-term outcomes of rare tumor subtypes, assess the role of advanced imaging and endoscopic techniques in earlier detection, and establish the value of routine small bowel evaluation in suspected nonepithelial GI tumors. Given the rarity of primary GI melanomas and sarcomas, collaborative registries would facilitate more robust epidemiologic and therapeutic analyses, thereby supporting evidence-based management strategies.

Declarations

Ethics declarations

IEC Approval: The study was performed according to ethical parameters, after receiving the IEC approval.

Funding Statment

No funding was obtained for this study.

Consent to Participate

Informed consent to participate was obtained from all of the participants in the study and signed a consent form for our study participants.

Consent for publication

Not Applicable

All research involving human participants, human data, or human material was conducted in full compliance with the ethical principles of the World Medical Association Declaration of Helsinki

Conflict of interests

No conflict of interest declares.

Availability of data and materials (ADM)

On request to Corresponding author

Author Contribution

Sasmita Panda, Snigdha Rani Nahak, Conceptualization, methodology, investigation, data curation, and visualization.

Sasmita Panda, Mamita Nayak, Debasmita Mahanta, Sashibhusan Dash: Data curation, writing-review and editing, methodology, and investigation.

Sasmita Panda, Mamita Nayak, Debasmita Mahanta, Sashibhusan Dash: data curation, writing-review and editing, investigation, formal analysis and supervision.

Sashibhusan Dash: Data curation, writing, Methodology, review and editing.

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References

[1] Galkin VN, Maĭstrenko NA. Diagnostika i khirurgicheskoe lechenie neépitelial'nykh opukholeĭ zheludochno-kishechnogo trakta [Non-epithelial tumors of gastrointestinal tract: diagnosis and surgical treatment]. Khirurgiia (Mosk). 2003;(1):22-6.

[2] Khan J, Ullah A, Waheed A, et al. Gastrointestinal Stromal Tumors (GIST): A Population-Based Study Using the SEER Database, including Management and Recent Advances in Targeted Therapy. Cancers (Basel). 2022;14(15):3689.

[3] Ahmed M. Gastrointestinal neuroendocrine tumors in 2020. World J Gastrointest Oncol. 2020 Aug 15;12(8):791-807. doi: 10.4251/wjgo.v12.i8.791.

[4] George DM, Lakshmanan A. Lymphomas with Primary Gastrointestinal Presentation: A Retrospective Study Covering a Five-Year Period at a Quaternary Care Center in Southern India. Cureus. 2024 Dec 5;16(12):e75161. doi: 10.7759/cureus.75161.

[5] Sbaraglia M, Businello G, Bellan E, Fassan M, Dei Tos AP. Mesenchymal tumours of the gastrointestinal tract. Pathologica. 2021;113(3):230-251. doi:10.32074/1591-951X-309

[6] Burch J, Ahmad I. Gastrointestinal Stromal Tumors. [Updated 2022 Sep 26]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554541/

[7] Nishida T, Blay JY, Hirota S, Kitagawa Y, Kang YK. The standard diagnosis, treatment, and follow-up of gastrointestinal stromal tumors based on guidelines. Gastric Cancer. 2016 Jan;19(1):3-14.

[8] Akahoshi K, Oya M, Koga T, Shiratsuchi Y. Current clinical management of gastrointestinal stromal tumor. World J Gastroenterol. 2018 Jul 14;24(26):2806-2817.

[9] Joensuu H, Hohenberger P, Corless CL. Gastrointestinal stromal tumour. Lancet. 2013 Sep 14;382(9896):973-83.

[10] Du Y, Chang X, Li X, Xing S. Incidence and survival of patients with primary gastrointestinal melanoma: a population-based study. Int J Colorectal Dis. 2023 Mar 30;38(1):87. doi: 10.1007/s00384-023-04385-x.

[11] Shah NJ, Aloysius MM, Bhanat E, et al. Epidemiology and outcomes of gastrointestinal mucosal melanomas: a national database analysis. BMC Gastroenterol. 2022;22(1):178.

[12] Ghimire P, Wu GY, Zhu L. Primary gastrointestinal lymphoma. World J Gastroenterol. 2011;17(6):697-707. doi:10.3748/wjg.v17.i6.697.

[13] Gajzer DC, Fletcher CD, Agaimy A, Brcic I, Khanlari M, Rosenberg AE. Primary gastrointestinal liposarcoma-a clinicopathological study of 8 cases of a rare entity. Hum Pathol. 2020 Mar;97:80-93. doi:10.1016/j.humpath.2019.12.004.

[14] González Luna AJ, Cuevas Calla CV, Castrejón Cardona CD, Sánchez García JA, Hernández Ibarra R. Malignant Peripheral Nerve Sheath Tumor of the Rectum Characterized by Focal S100 Protein Expression. Cureus. 2025 Jul 3;17(7):e87235. doi: 10.7759/cureus.87235.

[15] Zhao ZH, Yang JF, Wang JD, Wei JG, Liu F, Wang BY. Imaging findings of primary gastric plasmacytoma: a case report. World J Gastroenterol. 2014;20(29):10202-10207. doi:10.3748/wjg.v20.i29.10202.

[16] Mahdi M, Afaneh K, Mahdi A, Tayyem O. Colonic Ganglioneuroma: A Rare Incidental Finding. Kans J Med. 2023;16(1):112-113. doi:10.17161/kjm.vol16.18859.

[17] Sapalidis K, Laskou S, Kosmidis C, et al. Symptomatic colonic lipomas: Report of two cases and a review of the literature. SAGE Open Med Case Rep. 019;7:2050313X19830477. doi:10.1177/2050313X19830477