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Hist And Tert	opathological Study Of Various Neoplastic Non-neoplastic Lesions Of Small Intestine At iary Care Centre Of South Gujarat	KEY WORDS: Tuberculous enteritis, Polyp, Adenocarcinoma, GIST, Neuroendocrine tumour, B Cell NHL.		
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Introduction: Small intestine, the longest part of digestive tract, makes up about 75% of the total length and can be affected by various developmental, inflammatory or neoplastic conditions. Non neoplastic lesions like abdominal tuberculosis are frequently seen in small intestine. Although small intestine is an uncommon site for tumour nearly twothirds of these tumours are malignant, with most of them being adenocarcinoma. Objective: To study the histopathology of various neoplastic and non-neoplastic lesions of small intestine and to evaluate their frequency and pattern with respect to age, sex, anatomical sites and clinical findings. Materials and Methods: This observational cross-sectional study was conducted on a total of 101 small intestinal specimens including biopsies and surgically resected specimen received for histopathological examination over a period of two years in the Department of Pathology affiliated with tertiary care hospital. In addition to Haematoxylin and Eosin staining, Immunohistochemistry and special stains were also done in required cases. Results: This study showed a male is to female ratio of 1.97:1. Peak incidence of cases was seen in the 31-40 years age group. Out of total 101 pathological lesions 87 cases were non -neoplastic that included Infective lesions like tuberculous enteritis, Inflammatory lesions like Non-specific Enteritis, Necrotising Enteritis and Congenital lesions like Meckel's diverticulum, Enteric Duplication cyst and Celiac disease while only 14 cases were neoplastic that included benign neoplastic lesions like various types of polyps and malignant neoplastic lesions like adenocarcinoma, GIST, neuroendocrine tumour and B cell NHL. Conclusion: This study showed a characteristic distribution of cases in the three different parts of small intestine and highlighted the clinical importance of timely detection of intestinal pathology by the means of detailed clinical study combined with radiological and histopathological examination.

INTRODUCTION

ABSTRACT

Small intestine, the longest part of digestive tract, makes up about 75% of the total length and more than 90% of the total mucosal surface area of the gastrointestinal tract.[1] It is the principal site for digestion and absorption of nutrients from ingested food. The organ can be affected by various developmental, inflammatory or neoplastic conditions.[2] Although non neoplastic lesions are more frequently seen in small intestine, the clinical presentation of these diseases are often vague and non-specific with few if any specific clinical signs until the disease is advanced. Diagnostic delay because of these reasons may lead to development of complications like those seen in case of abdominal tuberculosis.[3]

In spite of its huge length and large pool of dividing cells small intestine is found to be an uncommon site for tumour and there is world wide variation in the distribution of these neoplasms, which is attributed largely to exogenous factors rather than genetic factors.[2,4] However, nearly two-thirds of the small bowel tumours are malignant, with most being adenocarcinoma followed by neuroendocrine tumours, lymphomas and sarcomas."[5] Worldwide, malignant tumours of the small intestine make up less than 1.0 per 100,000 population making them rare and 50 times less common than those of large intestine.[6,7]

In the present setup this observational descriptive study was undertaken to document and analyse the demographic pattern, anatomical distribution and histopathological presentation of a broad array of non-neoplastic and neoplastic lesions of the small intestine that were received in the pathology department of a tertiary health care centre along with their clinical correlation.

MATERIAL AND METHODS

This observational cross-sectional study was conducted in Department of Pathology affiliated with tertiary care hospital over a period of two years. A total of 101 small intestinal specimens including biopsies and surgically resected specimen received for histopathological examination were studied. Ethical clearance was obtained from Institutional Ethical committee before the beginning of this study.

A detailed clinical history including age, sex, clinical presentation, examination findings, radiological investigations reports and provisional clinical diagnosis was collected. Detailed gross examination of received intestinal specimen was done including measurement of received portion of intestinal tract, detection of loss of mucosal rugosity, detailed examination of growth, constriction or ulceration if any including appearance, extent of pathological lesion, external surface (exophytic/infiltrative/annular), cut surface, colour and consistency of the lesion were noted. In cases where lymph nodes were received separately along with intestine specimen, they were examined for size, appearance and then processed accordingly.

The specimens were received in 10% formalin and fixed for 24 hours, processed for paraffin sectioning, stained by routine haematoxylin and eosin stains and histomorphological features were analysed under light microscopy. Special stains like Periodic acid Schiff (PAS), Ziehl Neelsen stain as well as Immunohistochemistry were performed as per diagnostic requirement.

All the small intestinal lesions were classified in appropriate categories, tumours were classified according to WHO Classification of Digestive system tumours, and reporting of histopathological findings was done according to CAP protocol for examination of resection and biopsy specimen

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small intestine.

The data was analyzed manually for frequency, distribution and percentages of lesions according to their type, anatomical site, presenting age group, gender predominance and clinicopathological correlation.

RESULTS

This study showed a wide age range of presentation, with the youngest case being that of an omphalocele from a 1day old male child, and the oldest being a case of intestinal obstruction from an 80 years old female. Out of 101 small intestinal pathological lesions, 67 cases (66.33%) were from male patients and 34 cases (33.66%) were from female patients resulting in a male to female ratio of 1.97:1. Peak incidence of overall cases was seen in the 31-40 years age group.

In the present study out of all the parts of small intestine namely duodenum, jejunum and ileum, ileum was found to be the most frequently affected site for pathological lesion with 58 cases (57.42%) reported from ileum only, out of total 101 cases in small intestine. Among total 101 cases, 87 cases (86.14%) were non -neoplastic lesions while only 14 cases (13.86%) were neoplastic lesions.

Out of total 87 non-neoplastic cases of small intestine abdominal pain was the commonest presentation as seen in 42 cases (48.27%) followed by abdominal distension that was seen in 20 cases (22.98%) and altered bowel habits that was seen in 16 cases (18.39%).

On the other hand, the neoplastic cases of small intestine had a different picture of clinical presentation where the most frequent clinical complain was altered bowel habits, found in 9 cases (64.28%) followed by weight loss, found in 5 cases (35.71%).

The Non-neoplastic lesions of small intestine were broadly categorized Into Infective, Inflammatory and Congenital lesions with majority being inflammatory lesions with 66 number of cases (75.86%) followed by Infective lesions with 13 cases (14.94%) and congenital lesions with 8 cases (9.20%).

 Table 1 : Categorisation of non-neoplastic lesions of Small

 Intestine

Type of Non-Neoplastic lesion	Number	Percentage
Infective	13	14.94 %
Inflammatory	66	75.86 %
Congenital	08	9.20 %
Total	87	100

The Infective lesions category of small Intestine was solely composed of Tuberculous enteritis having a total of 13 cases all of which were seen in the ileum with two involving both of ileum and jejunum. The youngest patient was 7-year-old male and the oldest one was a 60-year-old male. Common clinical presentations of the TB intestine cases were altered bowel habits and intestinal obstruction due to stricture formation. Histopathological examination showed ill formed and well formed granuloma, multinucleated giant cells, marked infiltration by chronic inflammatory infiltrates. In some of the cases Ziehl Neelsen stain highlighted presence of Acid-Fast Bacilli.

Majority of the Inflammatory lesions category of small intestine was composed of 38 cases of Non-specific Enteritis (43.68%) followed by 24 cases of Necrotising Enteritis (27.59%) and 4 cases (4.60%) of Enterocutaneous Fistula.

The Congenital lesion category of small intestine had total 8 cases being composed of 2 cases of Meckel's diverticulum (2.30%),2 cases of Enteric Duplication cyst (2.30%),2 cases of www.worldwidejournals.com

Celiac Disease (2.30%), one case of Intestinal atresia (1.15%) and one case of Omphalocele (1.15%).

Table 2: Histopathological distribution of Non-neoplastic

lesions of small intestine

		1	1
Type of Lesion		Number	Percentage
Infective	Tuberculous Enteritis	13	14.94 %
Inflammatory	Necrotising Enteritis	24	27.59 %
	Non-specific Enteritis	38	43.68 %
	Enterocutaneous	4	4.60 %
	Fistula		
Congenital	Intestinal atresia	1	1.15%
	Meckel's diverticulum	2	2.30 %
	Enteric Duplication	2	2.30 %
	cyst		
	Celiac Disease	2	2.30 %
	Omphalocele	1	1.15 %
Total Number of Cases		87	100

Among the 14 neoplastic lesions of small intestine, 3 cases (21.43%) were benign (tumour and polyp) and 11 cases (78.57%) were malignant. Benign neoplastic lesions consisted of 1 case (7%) each of Hamartomatous polyp, Inflammatory polyp and lipomatous polyp. The Malignant Neoplastic lesions category was composed by 7 cases of Adenocarcinoma (50%), followed by 2 cases of Gastrointestinal Stromal Tumour (GIST) (14%) and I case each of Neuroendocrine Tumour (7%) and B cell Non-Hodgkin Lymphoma (7%).

Table	3 :	: Histo	pathological	Distribution	Of	Neoplastic
Lesior	ıs C	Of Smal	lIntestine			

Type of Lesion		Number	Percentage
Benign neoplastic	Hamartomatous	1	7%
lesions and	Polyp		
polyps	Inflammatory Poly	1	7%
	lipomatous polyp	1	7%
Malignant	Adenocarcinoma	7	50%
	Neuroendocrine	1	7%
	Tumour		
	BcellNHL	1	7%
	GIST	2	14%
Total Number of Cases		14	100%

DISCUSSION

Sex ratio for small intestinal lesions was 1.9:1 in studies conducted by Chennakeshaviah et al and Sampurna et al, which was similar to our study.[8] The highest frequency of small intestinal malignancy was observed in 31-40 years age group in both Sampurna et al and Saroj et al study, similar findings were also observed in present study.[9,10]

Though most of the non-neoplastic lesions of small intestine presented with complain of abdominal pain, the neoplastic lesions often showed paucity of significant clinical complains and presented with altered bowel habits and weight loss which often did not attract considerable clinical attention and went unnoticed by both the physician and the patient for a significant period of time. This resulted in delayed presentation and clinical intervention in many of the cases with small intestinal malignancies where the tumour reached a higher pathological stage with deeper invasion and showed local as well as distant metastatic spread rendering it difficult for surgical removal and therapeutic remission leading to poor prognosis and decreased life expectancy.

In this study out of total 101 cases of small intestine a majority of 58 cases (57.42%) were from ileum only. This observation was consistent with the studies conducted by Chennakeshaviah et al, Sampurna et al and Mural et al as in all these studies ileum was the most affected site of lesion in small intestine.[8,9,11]

In regard to the non-neoplastic lesions, in the Mural et al study

TB intestine was the only infective lesion in small intestine and was the commonest among all the non-neoplastic lesion with total 9 cases (32%) out of 28 non-neoplastic cases. In present study also infective lesion category is solely composed of TB intestine.[11]



Figure 1: Gross image Tuberculous Stricture in intestine (left) and microscopic image TB intestine (right) (H&E, 10x)

In regard to the benign neoplastic lesions different types of polyps, their proportions and comparison of the same with various studies is discussed below.

A single case of Hamartomatous polyp (7%) was received from the jejunum of a 19-year-old male patient. On histopathological examination it showed central core of smooth muscle and fibroconnective tissue covered by small intestinal mucosal epithelium with areas of calcification present at the base of stalk.

A case of Inflammatory polyp from the jejunum of a 17 years old male patient showed characteristic histomorphological features of an inflammatory polyp having mixed inflammatory infiltrate with dilated vascular channels in lamina propria and submucosa with eroded mucosa. In the Mural et al study 3.1% cases were found to be that of Inflammatory polyp.[11]

One case of Lipomatous polyp was received from the ileum of a 46-year-old male patient. Chennakeshaviah et al (2017) observed 3.77% cases of Lipomatous polyp in their study.[8] Mural et al (2020) observed 15.50% cases of Lipomatous polyp in their study.[11]

In the present study out of the 14 neoplastic lesions majority of the Malignant Neoplastic category was composed by Adenocarcinoma that had a total of 7 cases (50%) followed by 2 cases of GIST (14%). This category also included 1 case each of Neuroendocrine Tumour (7%) and B cell NHL (7%). In the study conducted by Wilson et al and Sethi and Hardin et al frequency of adenocarcinoma was the highest followed by Neuroendocrine tumour and Leiomyosarcoma.[12,13]

Out of the 7 cases of Adenocarcinoma of small intestine in the present study 5 were from duodenum and 2 were from ileum. Out of these 7 cases of Adenocarcinoma 5 were received as surgically resected specimens that showed exophytic growth pattern of tumour grossly and the rest 2 cases were received as biopsies.

There were two cases of Gastrointestinal Stromal Tumor (GIST). Both of these tumors had spindle cell morphology on microscopy and the tumour cells were immunoreactive for CD-117.



Figure 2: Gross Image (Left) And Microscopy Image (Right) Of Gist In Intestine (H & E, 10x)

A single case of B cell Non-Hodgkin Lymphoma was observed from an 11-year-old male patient which on gross examination showed a globular mass in jejunum and on histopathological examination showed partial to complete effacement of mucosa architecture along with diffuse effacement of submucosa, muscularis propria & serosa by proliferation of monomorphic lymphoid cells. On Immunohistochemistry tumour cells showed strong diffuse immunoreactivity for CD20.



Figure 3: Gross Image (Left) And Microscopic Image (Right) Of Non-hodgkin'slymphoma (Plasmablastic Type)OfTransverse Colon(h&e, 40x)

A single case of Well Differentiated Neuroendocrine Tumour was found which showed monotonous small round tumour cells arranged in solid nests separated by thin fibrous septae and few cells arranged in trabecular pattern. On Immunohistochemistry tumour cells were immunoreactive for synaptophysin and chromogranin.

CONCLUSION

A wide age range starting from neonatal period to late adulthood was covered in this study and it showed a characteristic histopathological distribution of cases in the three different parts of small intestine. In small intestine neoplastic lesions were significantly infrequent compared to non-neoplastic lesions. Among all the neoplastic lesions throughout the small intestine adenocarcinoma had the highest frequency.

The present study highlights the importance of timely detection of intestinal pathology by the means of detailed clinical examination, record of medical history orchestrated with radiological and pathological investigations. Histopathology being the gold standard of investigation for diagnosis of intestinal lesions, early detection of pathology in a small bit of intestinal biopsy tissue as well as proper typing, staging and grading of tumour in a surgically resected specimen can go a long way in reducing the disease burden in patients.

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