

A Histopathological Study of the Small Intestinal Lesions

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ABSTRACT

Introduction: Frequently received specimens of small intestine are non-neoplastic diseases like Crohn's, ischemic enteritis, non-specific enteritis, tuberculosis and neoplastic diseases like adenomas and carcinomas. Clinical and radiological findings are non specific and histopathological study is required for the diagnosis.

Aim: To study histomorphology of small intestinal lesions and analyze with respect to age, sex, anatomical site of occurrence and relative frequency.

Materials and Methods: This study of 124 cases was undertaken in the Department of Pathology, JSS Medical College and Hospital, Mysuru, India, between 2009 to 2012. In addition to H and E, Immunohistochemistry and special stains were done in required cases.

Results: Total 124 cases of small intestinal lesions including the periampullary lesions were studied. Of these, 71 cases

(57.25%) were non-neoplastic and 53 cases (42.75%) were neoplastic. Common age group was 5th-6th decade. A male preponderance was observed. Most common non-neoplastic lesions were non-specific enteritis (52.11%) and enteric fever (40%). Amongst neoplastic lesions, total 45 (84.91%) cases were malignant comprising adenocarcinomas of the periampullary region (49.06%) and carcinoid tumours (11.32%). Benign lesions were adenomas. Rare cases like myeloid sarcoma, metastatic adenocarcinoma and metastatic malignant melanoma were observed.

Conclusion: A greater awareness of various diseases affecting the small intestine and an understanding of the pathogenesis on the part of the pathologist is felt necessary for a better diagnosis. A detailed histopathological study of the small intestinal specimens should be done in constant correlation with the clinical and radiological findings for an accurate diagnosis.

Keywords: Brunner's adenoma, Carcinoid, Metastatic melanoma, Non-neoplastic lesions, Periampullary adenocarcinomas

INTRODUCTION

Nearly 75% of the total length of the gastrointestinal tract is made up by small bowel and it constitutes more than 90% of the mucosal surface area [1]. Infections, inflammatory diseases, and tumours affect the small intestine accounting for a majority of diseases [2]. Symptoms of the gut disorders are often vague and signs of abnormality are a few, unless the disease is advanced. Analysis of the clues from the gut and the effect of its disease on the body are required for the diagnosis [3].

Inflammation of the small bowel is relatively common viz., specific infections-viral or bacterial and non-specific inflammation caused by chronic infection, inflammatory bowel diseases and the drugs. Earlier, only severe acute and chronic pathological conditions were brought to the attention through literature. Now, ileoscopy helps to demonstrate many forms of enteritis [4].

Interruption or reduction of the small bowel blood supply results in changes, which vary in severity from superficial mucosal necrosis to irreparable full thickness damage with necrosis [5].

Worldwide, malignant tumours of the small intestine make up less than 1.0 per 100,000 population and thus are rare [6].

Availability of data on this was not much till now, but for the publication of two voluminous studies by Pan SY et al., [7] (reported 1,609 cases) and Howe JR et al., [8] who reviewed the national cancer database in 4,995 patients with small bowel adenocarcinoma. Nearly, two-thirds of the small bowel tumours are malignant, with most being adenocarcinoma; other types of tumours are carcinoids, lymphomas and sarcomas. Most tumours originate in duodenum (55.2%), followed by jejunum (17.6%) and the ileum (13%) [9].

The significant rise in the incidence of these tumours is an

important epidemiologic finding. Thus, the present study was conducted to find out the profiles of various histological lesions of the small intestine.

AIM

To study the histomorphology of all the small intestinal lesions in adults and to determine the pattern of the small intestinal lesions with respect to age, sex, anatomical site and relative frequency.

MATERIALS AND METHODS

The present study (Prospective and retrospective) was undertaken in the Department of Pathology, JSS Medical College and Hospital, Mysuru, India, from 2009 to 2012. Total 124 small intestinal specimens received for the histopathological examination were studied. The specimens were preserved in 10% formalin and fixed for 24 hours, processed for paraffin sectioning, stained by routine haematoxylin and eosin stains and histological features were analyzed. Immunohistochemistry was done in required cases like C-kit, CD34, CD43 and CD163 for myeloid sarcoma and HMB-45 for malignant melanoma and others like CD3, CD20, CD138, tdt, CD30 and Mic2 were also used and special stains like Zeil-Neelson for AFB, PAS, PAS with diastase and alcian blue for mucin were done in required cases to confirm the histopathological diagnosis. Bleaching was also done to confirm melanin pigment in metastatic melanoma.

Ethical clearance was obtained from Ethical committee, JSS Medical College, JSS University, Mysuru, India.

All endoscopic biopsies and resected specimens of small intestine of adult age group sent for histopathological diagnosis were included.

Cases belonging to < 18 years of age and inadequate biopsies were excluded.

The data was analyzed manually for frequency, distribution and percentages.

RESULTS

Total 124 cases of small intestinal lesions were studied. Of these, 71 cases (57.25%) were non-neoplastic (common non specific enteritis) and 53 cases (42.75%) were neoplastic (Common were benign-adenoma, Malignant - periampullary carcinoma). Patients in 5th-6th decade of life were most commonly affected showing male preponderance (the male to female ratio is 1.9: 1) [Table/Fig-1,2].

The most common site involved by small intestinal lesions was the ileum (42.45%). The common clinical features observed in order of frequency were pain abdomen (70.16%), jaundice (25%), vomiting (20.97%) and fever (8.06%) [Table/Fig-3].

Various clinical, histological and pathological specimens has been depicted in [Table/Fig-4-8].

DISCUSSION

Non-neoplastic Lesion	Number of Cases	Percentage
Inflammatory Lesion	62	87.32%
Enteric Fever	6	8.45%
Tuberculosis	3	4.23%
Crohn's Disease	5	7.04%
Nonspecific Enteritis	37	52.11%
Necrotising Enteritis	10	14.08%
Duodenal Ulcer	1	1.41%
Diffuse Villous Atrophy	1	1.41%
Hamartoma	1	1.41%
Ischaemic Bowel Disease	07	9.86%
Total	71	100%

[Table/Fig-1]: Distribution of non-neoplastic lesions of the small intestine.

Neoplastic Lesions	Number of Cases	Percentage
Benign	8	15.09%
Adenoma	4	7.55%
Lipoma	2	3.77%
Low Grade Dysplasia	1	1.89%
Brunner Glandadenoma	1	1.89%
Malignant	45	84.91%
Periampullary Adenocarcinoma	26	49.06%
Adenocarcinoma	3	5.66%
Carcinoid	6	11.32%
Gastro Intestinal Stromal Tumour	4	7.55%
Myeloid Sarcoma	1	1.89%
Metastatic Adenocarcinoma	1	1.89%
Metastatic Malignant Melanoma	1	1.89%
Poorly Differentiated Carcinoma	2	3.77%
Lymphoproliferative Disorder	1	1.89%
Total	53	100%

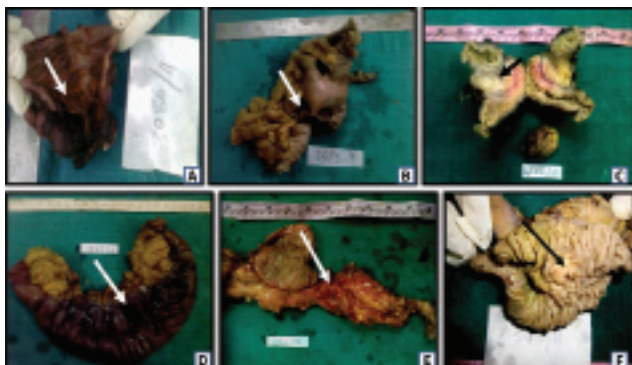
[Table/Fig-2]: Distribution of neoplastic lesions of the small intestine. [Including periampullary region neoplasms]

SI No	Symptoms	Number of Cases	Percentage
1	Pain Abdomen	87	70.16%
2	Jaundice	31	25.00%
3	Vomiting	26	20.97%
4	Fever	10	8.06%
5	Mass Per Abdomen	8	6.45%
6	Weight Loss	5	4.03%
7	Diarrhoea	4	3.23%
8	Constipation	2	1.61%
9	Aneamia	1	0.81%

[Table/Fig-3]: Distribution of various clinical symptoms of small intestinal lesions.

Etiology	Agarwal N et al., [10] study	Present study
Inflammatory	98.75%	96.55%
Neoplastic	1.25%	3.45%
Total	100%	100%

[Table/Fig-4]: Comparison of etiological classification of small intestinal perforation.



[Table/Fig-5a-f]: (a) Non specific enteritis- Cut section showing stricture (arrow) and focal areas of loss of mucosal folds; (b) Tuberculosis of ileum: Multiple perforations (arrow) are seen in the terminal ileum; (c) Ileocecal adhesion (arrow); (d) Gangrene (arrow) of the ileum; (e) Crohn's disease: Cut section showing multiple strictures (arrow); (f) Adenocarcinoma of periampullary region: Cut section showing a proliferative growth (arrow).

The commonest gross pathological finding observed was perforation in comparison with the study done by Agarwal N et al., [10] [Table/Fig-4]. A Case of ileocecal adhesion [Table/Fig-5c] and Gangrene [Table/Fig-5d] were seen.

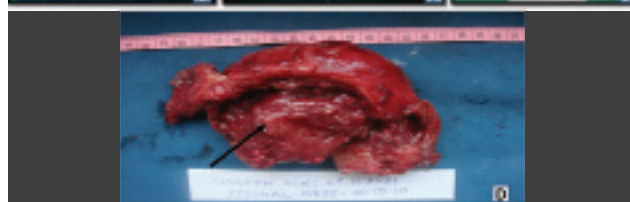
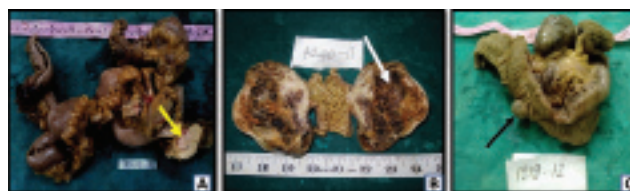
Clinical Significance: Symptoms can vary from vague abdominal pain to severe acute abdomen, Jaundice, vomiting, mass per abdomen, loss of weight, diarrhea, constipation and anemia. Hence small intestinal lesions also are to be considered in investigating a case with any of the above signs or symptoms.

Enteric Fever: The commonest clinical presentation was pain abdomen with signs of peritonitis (in 100% of cases).

In the present study 27 cases of perforation were observed including typhoid perforation 6 cases (22.28%), non specific ulcer perforation in 20 cases (76%) and tubercular perforation in 1 (14.28%) as compared to similar studies by Khan S et al., [11] [n= 18, typhoid perforation-7 (38.9%), non specific ulcer-5 (27.8%), tubercular perforation-2 (11.1%)]. Another study by Eid HO et al., suggested that non-traumatic perforation of the small bowel is an uncommon serious complication associated with high morbidity and mortality [12].

Tuberculosis: The commonest site of tuberculosis was ileum [Table/Fig-6b,8b].

Three patients presented with intestinal obstruction. Similar findings were observed by Dasgupta A et al., and Iqbal et al., [13,14]. Of the three patients, one had past history of pulmonary Koch's. Two cases (66.66%) showed epithelioid



[Table/Fig-6a-d]: (a) Carcinoid tumour: Cut section showing multiple well circumscribed yellowish tumour (arrow) in jejunum; (b) GIST: Cut section showing well circumscribed grey white tumour in jejunum with cystic change and areas of haemorrhage (arrow); (c) Metastatic malignant melanoma: Cut section showing polypoidal growth (arrow) in the mucosa of the ileum and mesenteric nodules of tumour; (d) Myeloid sarcoma: Cut section of the resected segment of the jejunum showing a mass (arrow) measuring 10X8 cm.

granulomas. Caseating and non-caseating granulomas were observed. A study by Pulimood et al., [15] found the following histopathological features specific for tuberculosis, and were used to differentiate between tuberculosis and Crohn's disease-

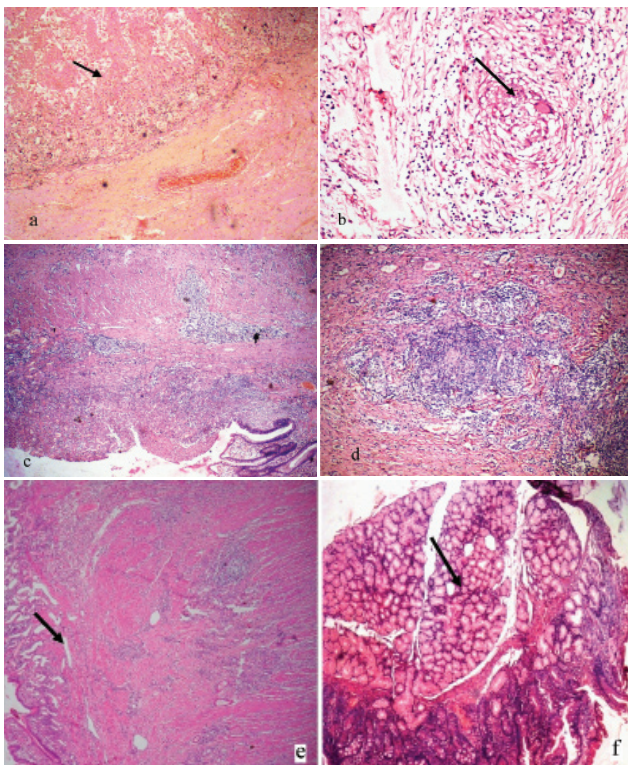
- Caseation
- Confluent granulomas
- Lymphoid cuff
- Granulomas larger than 400 micrometer
- 5 or more granulomas in biopsies from one segment
- Granulomas located in the submucosa or granulation tissue: often with palisaded histiocytes.
- Disproportionate submucosal inflammation

Crohn's disease: In our study 5 cases of Crohn's disease were studied which showed a male preponderance. Patients were mainly in 4th-5th decade [Table/fig- 5e,7c,7d].

Histopathology showed transmural lymphoid infiltrate, submucosal oedema, and granulomas in 3 cases (60%) which were non-caseating and discrete. In Crohn's disease, granulomas are discrete, and the lymph node do not show granuloma if none are seen in the intestine. In contrast, the granulomas in tuberculosis are confluent and could be found in lymph node even if the intestine shows none [15].

There were difficulties in distinguishing Crohn's disease from tubercular enteritis. A fact observed by Dutta AK et al., [16], Navaneethan U et al., [17]. Pulimod A et al., [15] described the granulomas which are Small (<200 micrometer), discrete, very few / single, poorly organized, Commonly located in the mucosa along with crypt centric inflammation and with aggregates of histiocytes. Microgranulomas helped in diagnosing Crohn's disease.

Duodenal Ulcer: One case was observed which presented



[Table/Fig-7a-f]: (a) Ischaemic enteritis: Tissue section showing mucosal coagulative necrosis (arrow), haemorrhage, acute inflammatory infiltrate and congested blood vessels. (H&E, 100x); (b) Tuberculosis: Tissue section showing confluent epithelioid granuloma (arrow) with Langhans' giant cell in submucosa. (H&E, 400x); (c) Crohn's disease: Tissue section showing transmural lymphoid aggregates (H&E, 10x); (d) Crohn's disease: Tissue section showing transmural inflammation (arrow); (H&E, 100x); (e) Neuro fibro vascular hamartoma: Tissue section showing tightly packed thin walled vascular channels in the mucosa (arrow) with ulceration, and expanded submucosa. (H and E, $\times 40$); (f) Brunner's gland adenoma: Tissue section showing lobules of Brunner's glands separated by intervening fibrous septa. (H&E, 10x).

with pain abdomen. Microscopic examination showed a surface coat of purulent exudate, and necrotic debris, fibrinoid necrosis, granulation tissue and fibrosis replacing the muscle wall and extending into the subserosa.

Non-Specific Enteritis: In present study both resected and endoscopic specimens were studied. Clinical diagnosis varied from peritonitis, secondary to perforation/tuberculosis/Crohn's to a tumour. Most of them presented with pain abdomen and signs of peritonitis. But on histopathological examination, the findings did not match the criteria of tuberculosis or Crohn's or tumour and some vague lesions like patchy ulceration, sub-mucosal oedema, congestion and mixed inflammatory infiltrate were found [Table/Fig-5a].

Necrotising Enteritis: Total 10 cases of necrotising enteritis were studied, most of them involving ileum, presenting with hyponatremia, metabolic acidosis and perforation peritonitis [Table/Fig-7a].

Histopathological findings were necrosis from mucosa and to

serosa without obstruction of the mesenteric vessels similar to findings by Zachariah SK et al., [18].

Neuro Fibro Vascular Hamartoma: Unusual lesions causing intestinal strictures and presenting as recurrent small bowel obstruction or chronic gastrointestinal (GI) bleeding are quite a few neuromuscular and vascular hamartomas.

Inflammation and narrowing were noted in the terminal ileum segment measuring 7 cm in length with dilatation of the proximal segment. Microscopically, there was mucosal ulceration with broadening of the villi, tightly packed thin-walled vascular channels and extensive crypt hyperplasia. There was an expansion of submucosa by disorganized bundles of smooth muscles in continuity with thickened muscularis mucosa [Table/Fig-7E].

As reported in some studies by Krishnamurthy V et al., [19]. Similar pathological features may be seen as part of the histological spectrum of Crohn's disease, radiation and ischemic enteritis [20]. Thus, it was concluded that NMVH, in isolation, as a relatively non specific change, is probably related to the chronicity of the disease.

Ischaemic Bowel Disease: Seven cases of ischemic bowel disease involved ileum - due to occlusion of mesenteric vessel (by thrombosis) and non occlusion in which no specific cause was there. Of these seven cases two cases were due to occlusive cause i.e., mesenteric vessel thrombosis and these patients presented with severe abdominal pain [Table/Fig-7a]. These two patients were in 6th and 8th decade similar to the findings observed by many authors.

Five cases of our study were due to non occlusive cause. Male to female ratio was 4:1. Abdominal pain was the constant feature and all the patients belonged to 4-5th decade. These findings are similar to the observations by Takeuchi et al., study [21].

Microscopically, gangrene and perforations were observed with ulcerations, haemorrhage and necrosis.

Benign Neoplastic Lesions: Adenomas (tubular and villous-periampullary region), Lipomas- in ileum and jejunum (presenting with intussusception) were studied.

One case of Brunner's gland adenoma presented with abdominal pain as a polypoidal lesion in the duodenal posterior wall and displayed Brunner's gland hyperplasia, forming lobules with intervening strands of fibrous tissue [Table/Fig-7f].

Malignant Lesions: Total 45 cases of malignant lesions including periampullary carcinomas were studied. periampullary adenocarcinomas being majority (57.77%), and 3 cases (6.66%) were of adenocarcinoma, 6 cases (13.33%) were of carcinoid, 4 cases (8.88%) of GIST, and one case each of myeloid sarcoma, metastatic adenocarcinoma and metastatic malignant melanoma.

Adenocarcinoma: Were the commonest malignancy type accounting for 64.44% and the commonest site was the 2nd part of duodenum in the periampullary region [Table/

Fig-5f,8a,8d]. Similar to observations by Terada T [22] and Dabaja BS et al., [23] 13 out of 16 Cases were whipple's resections and showed ulcerative to proliferative growth in the duodenum.

Histologically, 9 cases (56.25%) were moderately differentiated and 4 cases (25%) were well differentiated and 3 cases (18.75%) were poorly differentiated. Hong SH et al., [24] observed moderately differentiated adenocarcinoma as the common type similar to the present study.

One case of papillary adenocarcinoma and 3 cases of mucin secreting adenocarcinomas were studied in the present study.

Carcinoid Tumour: Total 6 cases of carcinoid were studied (4th-7th decade with a male to female ratio 2:1) and were the second most common (13.33%) and duodenum was the most common site (83.33%). One case (16.34%) showed involvement of jejunum and ileum [Table/Fig-6a,8b,8c]. Terada T [22] studied metastatic adenocarcinoma as second most common malignancy in variance with the present study. Age group was between 4th-8th decade and male to female ratio was 2:1 similar to the present study observations. Histologically all cases were Typical carcinoids with 'salt and pepper' chromatin, the cells arranged in trabecular and

insular patterns.

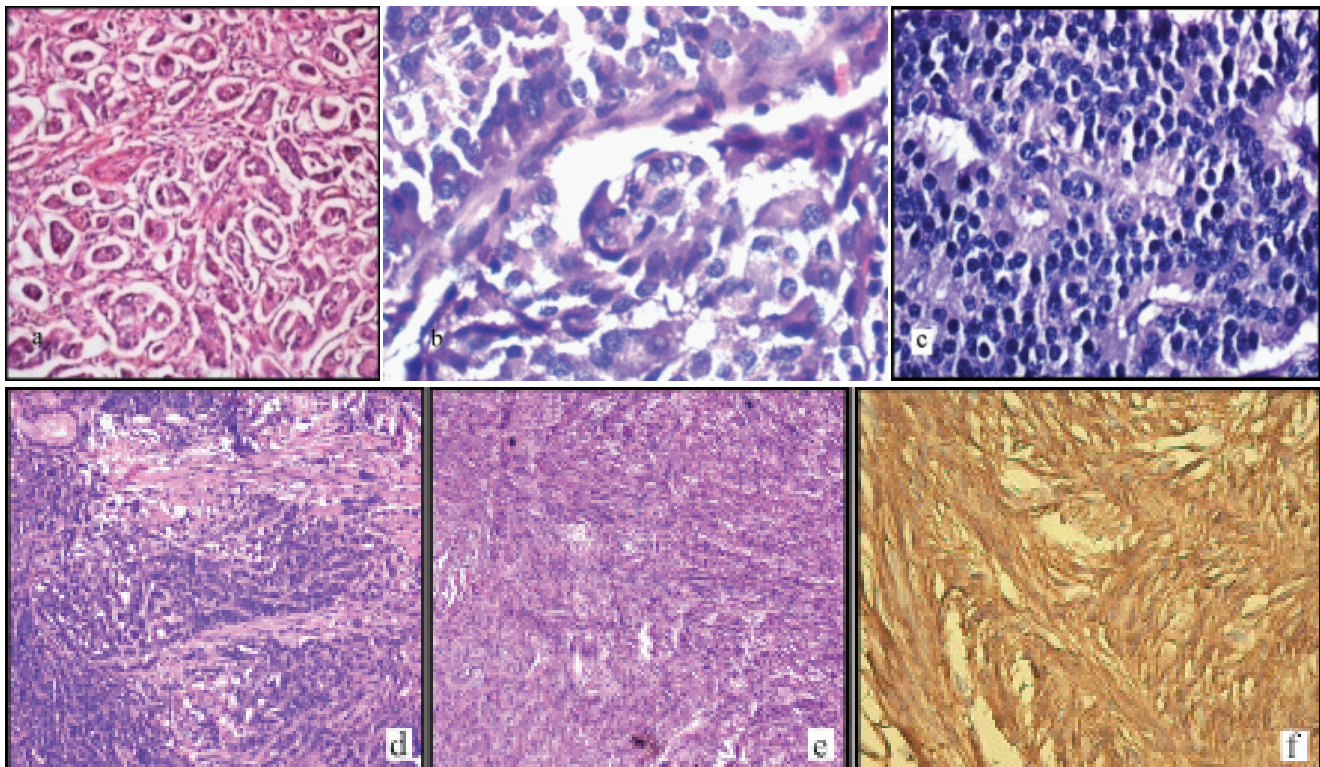
GIST (Gastrointestinal Stromal Tumour): Total 4 cases of GIST were studied with a male to female ratio of 3:1 and in 4th-6th decade. Jejunum was involved in all cases (100%) [Table/Fig-6b,8e,f]. Farhat MH et al., in their study observed similar results with respect to age, sex, and site [25].

Myeloid Sarcoma: Myeloid sarcoma is a tumour mass consisting of myeloblasts with or without maturation occurring at an anatomical site other than bone marrow and are uncommon in small intestine and represent 1%-2% of all the gastrointestinal neoplasms.

One case of myeloid sarcoma in proximal jejunum was studied. An 18-year-old male patient presented with nausea for the past 15 days, mass in the left iliac fossa, abdominal distension and vomiting. A clinical diagnosis of intussusception was made [Table/Fig-6d]. Similar findings were observed by Jung SH et al., [26].

- Microscopic examination showed round to oval tumour cells with scant cytoplasm, irregular vesicular nuclei with prominent nucleoli infiltrating all the layers.

Tumour cells expressed Ckit, CD34, CD43 and CD 163, while they were negative for CD3, CD20, CD138, tdt, CD30



[Table/Fig-8a-f]: (a) Moderately differentiated adenocarcinoma: Tissue section showing tumour cells in glandular pattern and infiltrating muscularis propria; (b) Carcinoid tumour: Tissue section showing a well circumscribed tumour in the submucosa, with cells arranged in tubular pattern. (H&E 40x); (c) Carcinoid tumour: Tissue section showing tumour cells with salt and pepper type chromatin. (H&E, 400x); (d) Poorly differentiated carcinoma: Tissue section showing tumour cells in sheets (arrow) infiltrating muscularis propria. (H&E, 200x); (e) GIST: Tissue section showing Intersecting fascicles of bland spindled cells (H & E (X200)); (f) GIST: Cytoplasmic reactivity is observed in neoplastic cells diffusely with membranous accentuation present for CD117 (CD117 X400).

and Mic2.

Metastatic Adenocarcinoma: One case (0.8%) of metastatic adenocarcinoma to ileum was observed similar to the results of Terada T [22]. A 70 years old male patient presented with pain abdomen and signs of peritonitis. Clinical diagnosis of peritonitis secondary to ileal perforation was made. Microscopy showed an infiltrating tumour tissue arranged in glandular pattern and infiltrating the full thickness of the intestinal wall. Lymphovascular emboli and perineural invasion was also observed.

Primary site was not made out in the present study.

Terada T, found 6 cases of metastatic adenocarcinoma in their study - 2 cases had origin in pancreas and one each from ovary, gall bladder, lung, and colon [22].

Metastatic Malignant Melanoma: Metastatic malignant melanoma in the small bowel is uncommon. One case of metastatic malignant melanoma with the primary in the rectum was observed. A 31 year old male presented with pain abdomen was opined clinically as intestinal obstruction. Resected segments of jejunum and ileum with mesentery showed a nodular growth in ileum with multiple nodules in the mesentery [Table/Fig-6c].

Microscopy showed a malignant tumour composed of round to polygonal cells in an organoid pattern, nests and sheets infiltrating all layers. A few spindle cells with scant clear to eosinophilic cytoplasm and irregular nuclei were seen. IHC showed HMB 45 positivity.

After 10 days of primary surgery, the patient was found to have a rectal growth and resected. Histopathology showed features of malignant melanoma.

Lens M et al., report that malignant melanoma cases presented with bowel metastases before death in 5% of the cases [27].

Lymphoproliferative Disorder: One case of lymphoproliferative disorder was observed in a 70 years old female who presented with anemia and endoscopy showed multiple nodules involving the stomach, duodenum, and jejunum. Microscopy showed an expansion of lamina propria by lymphoid infiltrate composed of small to medium sized cells infiltrating the muscularis mucosa with occasional lymphoid follicles.

Terada T in their study observed six cases of lymphomas in the range of 69-72 years and all cases involved ileum and with a male to female ratio of 2:4 [22].

LIMITATIONS

Paediatric age group was not included in this study. This group can also present with the same signs and symptoms and similar lesions can be found. Periapillary lesions studied can arise even from the bile duct and Pancreatic ducts. Not many studies are available on the study of lesions of small intestine.

CONCLUSION

Disorders of the small intestine account for a large portion of the human diseases. Infections, inflammatory diseases, and tumours affect it.

There are only a few comprehensive studies of small intestinal lesions. The clinical features and radiological findings are non-specific in various diseases and thus histopathological study becomes a must in confirming the diagnosis.

The incidence of small intestinal malignancy involving periampullary region is increasing progressively. A greater awareness of various diseases affecting the small intestine and an understanding of the pathogenesis on the part of the pathologist was felt necessary for a better diagnosis. A detailed histopathological study of the small intestinal specimens should be done in constant correlation with the clinical and radiological findings for an accurate diagnosis.

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