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Primary jejunal adenocarcinoma – A mute assassin

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Abstract
Small bowel tumors are rare, accounting for only 3-6% of gastrointestinal (GI) neoplasms, 12% of them being malignant. The most common histologic subtype is adenocarcinoma. Primary jejunal adenocarcinoma constitutes a very small portion of small intestinal adenocarcinoma. Clinical manifestations of this entity occur in advanced stages of its progression and it is often difficult to diagnose. It presents with nonspecific symptoms. Prognosis is not good usually. Surgical resection is the treatment of choice at early stage, however no standard protocol has been established for chemotherapy in unresectable or metastatic disease.
Case Report: We report a rare case of Primary jejunal adenocarcinoma in a 65 year old female presenting with long standing anemia and generalised weakness. Various investigations like Upper Gastrointestinal (GI) Endoscopy, Colonoscopy, Contrast enhanced computed tomography (CECT) of whole abdomen were done, but the exact location of the tumor could not be determined preoperatively. Exploratory laparotomy was performed, which revealed a cystic mass in the proximal jejunum. Segmental resection of the part of jejunum containing the cystic mass was done along with regional lymph node resection. Histopathological examination of the resected specimen was done and a diagnosis of Adenocarcinoma was made.
Conclusion: Primary small bowel adenocarcinoma, more precisely Primary jejunal adenocarcinoma is a rare entity and frequently presents with non specific clinical symptoms.
Most cases are diagnosed during laparotomy. Surgical resection is the treatment of this tumor.

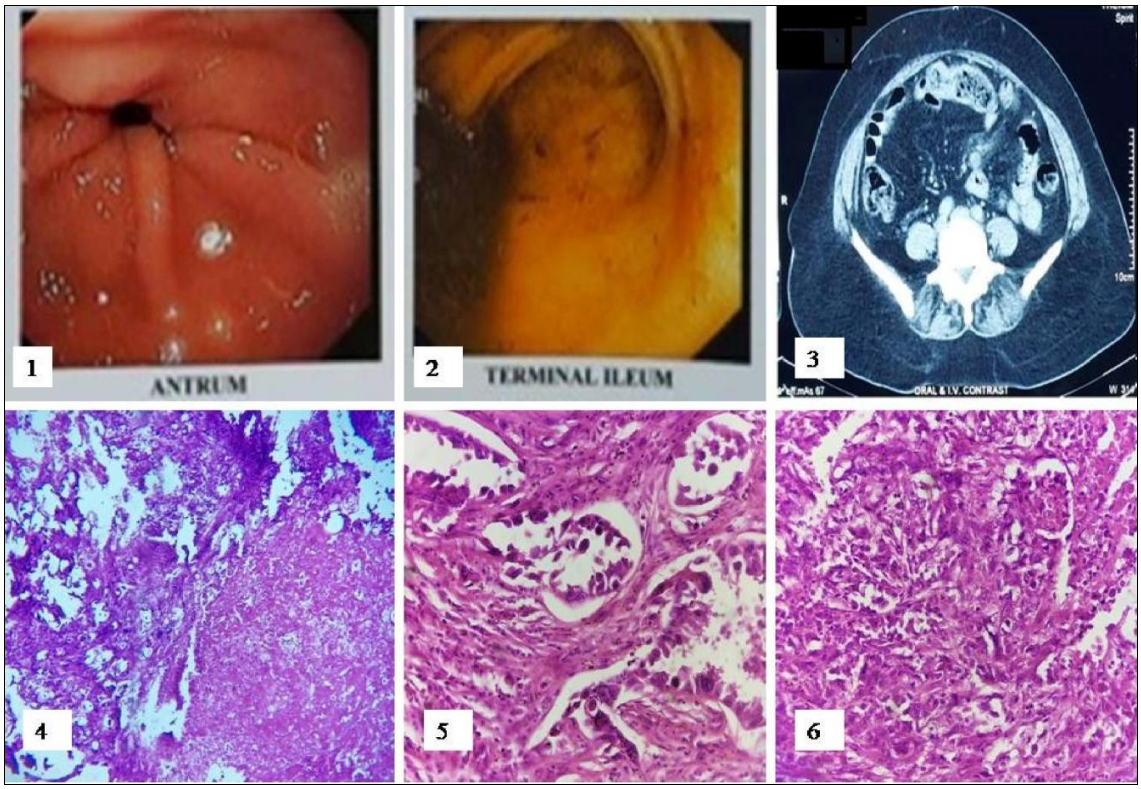
Keywords: Colonoscopy, contrast enhanced computed tomography, exploratory laparotomy, jejunal adenocarcinoma, upper gastrointestinal endoscopy, surgery

Introduction
Small bowel tumors are uncommon worldwide. They form 3%-6% of GI neoplasms, among which 1%-2% are malignant [1, 2]. There are four common histological types of small bowel tumors.
adenocarcinoma (30-40%), carcinoid tumor (35-42%), lymphoma (15-20%) and sarcoma (10-15%) [3]. A large proportion of small bowel malignancy is duodenal adenocarcinoma (57%), while primary jejunal adenocarcinoma comprising of 29% and primary ileal adenocarcinoma are rarely encountered forming only 10% [4]. The estimated annual incidence of small bowel cancer is 0.56 cases per 100,000 persons, with a higher prevalence rate in the black population than the whites [5, 6]. It is common in males compared to females [5, 6]. It is most frequently diagnosed among people aged 55-64 years and usually occurs after the age of 40 years. It is challenging to diagnose small bowel adenocarcinoma (SBA) preoperatively mainly due to its wide ranging clinical presentations and difficult endoscopic access to the
duodenum and jejunum. The patients present with vague symptoms of abdominal pain, nausea, vomiting, anemia, bleeding and signs of obstruction. Double Balloon Enteroscopy may be of some help in dignosing these tumors before biopsy [7]. Due to difficulty in the access of endoscopy the diagnosis of SBA is often delayed, missed or only detected at advanced stages. More than 50% of cases are diagnosed during laparotomy [8].
Complete surgical resection is the treatment of choice in the early stage and the role of adjuvant therapy remains uncertain [4].

Here we are presenting a rare case of Primary jejunal adenocarcinoma in a 65year old woman with one year history of gradually progressive generalised weakness and anemia.

Case Report
A 65-year-old woman came to the out patient department with the history of gradually progressive generalised weakness for one year and it was associated with exertional dyspnoea in later stage. The dyspnea started at rest three months prior to surgery. She was diagnosed with anemia. She also gave a history of weight loss of 8 kg within that one year duration. She denied of having abdominal pain, nausea, vomiting, post prandial fullness, hematemesis and malena and any signs of bowel obstruction. Physical examination did not show any abnormality. There was no significant past medical or sugical history or family history.
Laboratory investigations revealed normocytic normochromic anemia (Hb-6.3g/dl). Her serum chemistry and liver function tests were within normal limits. Examination of tumor associated antigens showed high levels of carcinoembryonic antigen (CEA) and carbohydrate antigen (CA 19-9).
Upper GI endoscopy revealed hiatus hernia, antral erosion (Fig.1). Urease test was negative. Colonoscopic examination revealed normal study (Fig.2). Capsule Endoscopy (CE) was not available, whole abdomen CECT was done which revealed a 3.5mm left mid abdominal cystic lesion (probably neoplastic) with adjacent small bowel wall thickening (Fig.3).

Subsequently, the patient underwent exploratory laparotomy and a proximal jejunal cystic mass was identified intraoperatively. Segmental resection of the jejunum was done along with primary anastomosis. The specimen was sent to the department of Pathology for histopathological examination. Postoperative recovery was uneventful.



1. Upper GI Endoscopy showing antral erosion.
2. Colonoscopy showing normal terminal ileal mucosa.
3. C.E.C.T. scan of whole abdomen showing mid abdomen cystic lesion with adjacent small bowel thinking.
4. H&E (40X) of jejunal mass showing tumor cell with desmoplastic stroma.
5. H&E (400X) of jejunal mass showing poorly formed glands lined by cells with high N:C ratio, hyperchromasia and pleomorphism.
6. H&E (100X) of jejunal mass showing poorly differentiated adenocarcinoma in a lymphocyte rich background

Histopathological examination confirmed the diagnosis of Adenocarcinoma NOS of jejunum Histological grade G3, (Poorly differentiated) invading through the muscularis propria reaching up to serosa. Lymphovascular invasion was present (Fig.4- 6). The radial margin was focally involved by invasive carcinoma. The proximal and distal margins were free. Two regional lymph nodes showing metastatic deposits of the adenocarcinoma were identified. T3N1M0.

At present the patient is doing well with normal Hemoglobin (12g/dl), Hematocrit (38%) and CEA (3.0 ng/dl) levels at 18 months follow up. Follow up with surveillance CT scan of chest, abdomen and pelvis at postoperative period of two years showed no recurrence. No adjuvant chemotherapy has been proposed till date in this case.

Discussion

The small bowel comprises 75% of the length of the entire digestive tract and 90% of its mucosal surface area. Small intestine is located between stomach at one end and colon at other end. The incidence of carcinoma is high in both stomach and colon but surprisingly the frequency of small bowel neoplasms is lower than in the stomach or the large bowel, accounting for about 3-6% of all gastrointestinal malignancies [9, 10]. This apparent neoplastic resistance has various hypothesized explanations. The liquid stool passes very quickly through the small intestine and there is minimal contact of carcinogens with it. The fast passage of food through small intestine provides low mucosal contact time, thereby reducing mucosal injury[11]. Low bacterial content of small intestine incapable of transforming food components into potential carcinogens, protective lymphoid tissue, presence of bile acids, rapid turnover of the epithelial cells contribute to protection against neoplastic lesions [11, 12].This rapid epithelial cell turnover in the small intestine is of estimated 1 g of intestinal mucosal cells being lost and replaced every 16 minutes and it prevents malignant change becoming established as cells containing DNA errors are rapidly lost.

The common presenting symptom is pain [12]. Most of the time it is diagnosed after surgery. Less than half of the cases are diagnosed prior to surgery [10]. T. Aparacio *et al* described 127 cases in which the clinical presentation of primary intestinal adenocarcinoma is nonspecific and includes vague symptoms of abdominal pain, nausea, vomiting, GI bleeding, weight loss and signs of obstruction. A few were diagnosed incidentally during surgery [13]. But in our case the patient did not complain about pain. She presented with weakness. Most common genetic mutation was P53 followed by KRAS. Mutation of APC was noted in a few cases [14].

Small intestinal adenocarcinoma comprises of 33% of small intestinal tumors. The other epithelial origin variants include mucinous adenocarcinoma, or the small cell, signet ring cell,

squamous and adenosquamous, medullary or even undifferentiated carcinoma are much rarer. The frequency of small bowel tumors is higher in the duodenum (50%) and decreases distally with 18% cases seen in the jejunum and 13-23.8% in the ileum [2, 13].

Risk factors for small bowel malignancies include smoking, alcohol consumption, consumption of red meat, smoked or salted food. (Lynch syndrome), familial adenomatous polyposis, Peutz Jehgers syndrome and Cystic fibrosis. The incidence is also increased in small bowel Crohn's disease, Coeliac disease and pre-existing adenoma [14]. There is increased incidence of SBA in inherited conditions like Familial adenomatous polyposis. SBAs are slightly more common in men than women and the mean age of diagnosis is over 60 years. Some cases were diagnose in Japan during screening for stomach carcinoma [14]. However, the patient may remain asymptomatic or present with weakness and anemia at the early stage, as in our case.

Accrding to Negri *et al*. this small intestinal adenocarcinoma is associated with the intake of rice, pasta, bread and red meat. But consumption of alcohol and smoking is not a risk factor. He also saw that having fish, vegetables, fruit lower the risk of developing adenocarcinoma [15]. But in our case she used to take normal Indian diet and there was no history of having alcohol and smoking.

The Primary small intestinal adenocarcinoma is associated with non specific symptoms. So it is usually difficult to diagnose preoperatively. In our case the patient presented with weakness, loss of weight and dyspnea. The jejunal adenocarcinoma in small intestine causes difficulty with endoscopic access. As a result, the diagnosis of jejunal adenocarcinoma and other small intestinal malignancies is usually delayed, missed or only detected at advanced stages with poor prognosis [16]. Studies have shown that SBA is usually diagnosed at late stage. Some of the patients had the previous history of leukemia, lymphoma, breast carcinma, prostate carcinoma [8]. Here our patient did not have any past history of any malignant tumor. The various diagnostic modalities available for detecting small bowel tumors include- CT scan of small bowel, enteroclysis, upper GI endoscopy, capsule endoscopy, push enteroscopy, double balloon endoscopy [16].

But as all are not available in our institution we had to rely on CECT- whole abdomen for preoperative diagnosis. CT scan has an accuracy of 47% for the diagnosis of SBA and is a valuable mode of investigation for detecting local, regional and distant metastasis; however, it may have role in diagnosing small primary lesions. While the CT scans can detect the lesions, they cannot provide precise data of the intestinal mucosa and may miss some small or flat lesions. In our case CECT whole abdomen was done preoperatively, but it could not detect the exact location of the tumor and the diagnosis was done intraoperatively and confirmed later on histopathological examination.

Both upper GI endoscopy and colonoscopy was done in our patient to look for any other tumors suggesting predisposing genetic disease, however, no other tumor was detected. Evaluation of tumor markers are important for assessment before and after surgery. There is no standardised adjuvant therapy for this tumor [16]. Serum tumor markers like CEA and CA 19-9 was found to be elevated in our case.

Surgical resection of the tumor with clear margins and regional lymph node resection is the treatment of choice in early SBA as it provides the best overall survival. Curative surgery offers a 50% chance of cure. However, failure following a curative surgery occurs when there is recurrence at distant sites following curative resection [11]. In our case segmental resection of the part of jejunum containing the tumor was done followed by end to end anastomosis. No adjuvant chemotherapy regimen was given to our patient till date. The prognosis of SBA is not good. It has been seen that average five year survival rate is related to the stage of the tumor. the satge IV tumor has the worst prognosis. In most cases the five year survival rate is 14% to 33%. The prognosis becomes even worse in male patients, and in persons above 55 years. The cases with lymph node metastasis and distant metastasis also play important role in overall survival. The primary jejunal or ileal tumor bear a better prognosis than primary duodenal tumor [16]. Effective adjuvant theray is not helpful in primary SBA [17].

Conclusion

Primary Jejunal adenocarcinoma is rare. While its clinical presentation remains nonspecific, it is important to remember that each case of anemia and weakness in elderly should be handled with care. Most of the cases of SBA are diagnosed during Laparotomy. Endoscopy and CT scan often miss it. CT enteroclysis and capsular endoscopy are of some help. Tumor markers like CEA and CA19.9 also help in diagnosing this lesion. Surgical resection with clear margins is the treatment of choice. The prognosis is poor if the diagnosis occurs in advanced stage. So far there is no standardised chemotherapy for this lesion.

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