Small Bowel Adenocarcinoma – Report of Two Cases and Review of Literature

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Abstract Although accounting for 90 % of the intestinal surface area, small bowel adenocarcinomas are not common. The majority of these lesions are incidentally detected during laparotomy for intestinal obstruction or perforation. The symptoms associated with these lesions are not very specific and preoperative diagnosis is rare. We report two cases of jejunal adenocarcinomas detected in patients undergoing laparotomy for acute abdomen and review the literature for small bowel adenocarcinomas.

Keywords Small bowel adenocarcinoma · Intussusception · Perforation · Diagnosis

Introduction

Carcinoma affecting the small bowel is not common. The usual pathologies found are carcinoids or lymphomas. Majority of these cases are diagnosed only when they present as acute abdomen in the form of intestinal obstruction or perforation. In some cases, they are diagnosed during evaluation of obscure gastrointestinal bleeding. We report two cases of acute abdomen with disease process involving the small bowel which on histopathology was diagnosed to be adenocarcinoma involving the small bowel and review the literature for the same.

Case Reports

We report two cases of acute abdomen with disease process involving the proximal jejunum which on histopathology was diagnosed to be adenocarcinoma involving the jejunum.

Case 1

A 60-year-old man with hoarseness of voice and a mediastinal mass on X-ray and CT chest was referred to the surgery casualty with complaints of abdominal pain and severe vomiting. He also had constipation. X-ray abdomen showed a few proximal dilated small bowel loops and absent gas shadows in the distal small and large bowels. Laparotomy was done for acute intestinal obstruction. A jejuno-jejunal intussusception with gangrenous changes in the apex of the intussusception was present. The patient underwent a jejunal resection anastomosis. The cut-open specimen showed a polyp at the apex of the intussusception and a few other polyps in the resected segment. There were no other palpable lesions in the rest of the bowel. The patient had an uneventful recovery and was referred to another center for the mediastinal mass. Histopathology of the specimen was reported as poorly differentiated carcinoma with cells arranged in sheets, cords and a vague adeno pattern infiltrating jejunum at multiple foci, possibility metastatic. The bronchoscopic biopsy of the mediastinal mass was reported as moderately differentiated squamous cell carcinoma.

Case 2

A 72-year-old man was referred from another hospital as a case of acute abdomen with peritonitis. He had tachycardia and a distended rigid abdomen. X-ray of the chest showed free air under the diaphragm. On laparotomy, a 0.5 cm

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perforation was identified on the antimesenteric border of the jejunum, about 1 ft from the duodenojejunal flexure. There was moderate amount of peritoneal contamination. A wedge resection of the ulcer was done with anastomosis in two layers. The patient developed a leak on the tenth post-operative day followed by adult respiratory distress syndrome and death. Biopsy of the wedge resection was reported as invasive adenocarcinoma infiltrating up to the muscularis layer.

Discussion

Epidemiology

The incidence of primary malignancies in the small bowel is low when compared with the colon [1]. The global incidence is less than one per 1,00,000 population [2]. Although accounting for about 75 % of the length of the digestive tract and 90 % of the intestinal surface area, small bowel tumors account for only about 3–6 % of gastrointestinal neoplasms [3]. The incidence rate of small bowel cancer is however increasing. The incidence increases with age and is higher in the male population [4]. One study found the mean age of incidence to be 53 years [3]. Other retrospective series have also found similar average age of presentation [5].

Four main histological subtypes have been described: adenocarcinomas, carcinoid tumors, lymphomas, and sarcoma [6]. One analysis of the National Cancer Data Base and Surveillance Epidemiology and End Results database found the following percentage distribution of histologic subtypes of small bowel cancer: carcinoid 37.4 %, adenocarcinoma 36.9 %, lymphoma 17.3 %, and gastrointestinal stromal tumor 8.4 % [7]. Adenocarcinomas were the commonest histologic subtype of malignant small bowel tumors (30–50 %). However, carcinoid tumors are more common now [8]. One study found a fourfold increase in carcinoid tumors but less for adenocarcinoma and lymphoma. Small intestine sarcoma showed stable rate of increase [6]. In the small intestine, the duodenum is at the highest risk of adenocarcinomas, while the ileum is at higher risk of carcinoids and lymphomas. Adenocarcinomas are more common in industrialized countries, while lymphomas are more common in the developing world [4].

Jejunal adenocarcinomas have been reported in literature, though all of them highlight the rarity of these tumors. A retrospective review of 42 patients with small bowel adenocarcinomas found the jejunum to be involved in 38 % of the cases. The duodenum accounted for 50 % and ileum 12 % of tumors [9]. Another multi-institutional study documenting 197 cases of small bowel adenocarcinomas found that around 30 % of these lesions were present in the jejunum [10]. A review of 69 patients with primary small bowel

tumors over a 15-year period showed the incidence of jejunal lesions to be 41 % with a 5-year survival of 34.28 % [5]. Han et al. evaluated the clinical presentation, treatment, and survival of patients with primary small bowel tumors. They found the ileum to be the most commonly involved site (44.7 %) followed by the jejunum (30.5 %) [11].

Etiopathogenesis

Various theories have been proposed to explain the relative rarity of small intestinal carcinomas. The rapid turnover of the intestinal mucosal cells results in shedding of cells before accumulation of genetic damage. The exposure of the mucosal cells to carcinogenic agents is also limited because of the rapid transit in the small bowel, lack of bacterial degradation activity from the lower bacterial load, and the relatively dilute alkaline environment of the small bowel [8]. Low levels of activating enzymes of precarcinogens may also be protective [4]. Some studies have demonstrated that the small intestine generates less endogenous reactive oxidative species (ROS) than the colon, enabling it to handle oxidative stress more effectively and hence less oxidative damage [12].

One prospective study on dietary risk factors did not find a clear association between red meat intake and adenocarcinoma or carcinoid of the small intestine. However, saturated fat intake was associated with elevated risk of small bowel carcinoids [13]. Vegetable diet with high fiber has a protective effect [14].

Cigarette smoking, alcohol intake, and other medical conditions such as Crohn's disease (CD), familial adenomatous polyposis (FAP), peptic ulcer disease, cholecystectomy, and cystic fibrosis are associated with higher risk of small bowel cancers [4].

Jejunal carcinoma has been reported in patients with FAP. Ruys et al. reported three patients with FAP who developed advanced duodenal adenomatosis and jejunal carcinoma which was associated with poor prognosis in two patients [15]. Patients with FAP have multiple adenomas in the small bowel, mainly the duodenum, which are associated with an increased risk of cancer [16]. Another autosomal condition, Peutz-Jeghers syndrome (PJS), is associated with polyps in the small intestine, with jejunum being the commonest site followed by the ileum and duodenum [17]. Small intestinal neoplasms may occur in association with PJS [18].

There are reports in the literature of association between CD and small bowel adenocarcinoma. A population-based case-control study to evaluate the association of CD (CD) with small bowel cancer in an elderly population found a strong association between CD and small bowel cancer; however, the prevalence of CD in patients with small bowel cancer was low. It is concluded that although CD is a

significant risk factor for small bowel cancers among older individuals, the absolute risk is small [19]. Recurrence of symptoms after relative quiescence and small bowel obstruction refractory to medical therapy was associated with small bowel adenocarcinomas [20]. Young age of onset and extended duration of the disease, distal jejunal and ileal location, male sex, small bowel bypass loops, strictures, and chronic fistulous disease are suggested to be associated with an increased risk of small bowel carcinoma in patients with CD [6].

The prevalence of adenomas in the small intestine is less than in the colon, but there appears to be a similar phenotypic adenoma–carcinoma transformation sequence [21]. However, one marked difference is the infrequent rate of mutations of the adenomatous polyposis coli (APC) gene. One study has highlighted that small bowel adenocarcinoma may follow a different genetic pathway compared to colorectal malignancies. A genetic analysis of 21 nonfamilial, nonampullary malignancies did not show mutations in the mutation cluster region of the APC gene. However, abnormal expression of E-cadherin and beta-catenin was found and may reflect an early alternative to APC in this pathway in which mutations may be found in adenocarcinoma of the small intestine [22].

Symptomatology and Diagnosis

The commonest symptoms were abdominal pain or discomfort followed by a mass. Only about 5 % patients presented with bowel perforation and peritonitis. Bowel obstruction, hematochezia, jaundice, and gastrointestinal bleed with shock were the other symptoms usually associated with small bowel tumors [11]. Another retrospective analysis found abdominal pain (48 %), anemia (39 %), and small bowel obstruction (33 %) to be the most common symptoms [23].

The diagnosis is usually made at laparotomy for small bowel obstruction or ulcer perforation. Rarely, small bowel adenocarcinomas may be diagnosed during evaluation of a small bowel bleed. However, it was difficult in previous years to evaluate the entire small bowel. Barium small bowel follow-through was used extensively in small bowel evaluation. Around 60 % sensitivity for diagnosis has been found in those with advanced small bowel disease, while small bowel enema (enteroclysis) shows a sensitivity of 95 %. It detects lesions even when the follow-through study has been normal [24].

Computed tomography (CT) and magnetic resonance imaging (MRI) have limited ability to identify primary lesions, but mesenteric infiltration, locoregional nodal involvement, and distant metastasis can be detected [25]. CT enteroclysis can also be used to increase the sensitivity for detecting small bowel lesions [26].

The endoscope in usual use cannot evaluate the length of the small bowel. Push enteroscopy using a long endoscope can examine the proximal 150–200 cm of the small bowel [8]. There are reports of preoperative diagnosis of jejunal tumors using double-balloon enteroscopy (DBE) [27]. Stenosis or ulceration is the most commonly observed findings on DBE [28]. However, this is not easily available and can be time-consuming.

Wireless capsule endoscopy is another method useful in evaluating the entire small bowel. It has been used in patients with obscure gastrointestinal bleeding where other investigations have been inconclusive [29]. A capsule endoscopy better visualizes and characterizes subtle mucosal lesions compared to magnetic resonance enterography (MRE). MRE yields better perienteric and extraenteric information. Both can be used as complementary methods [30].

Management

Complete resection offers the best chances of cure. In adult intestinal intussusception, resection without reduction is considered the optimal management if an underlying primary malignancy cannot be excluded [1]. Recent advances in capsule endoscopy, DBE, and single-balloon enteroscopy have led to better evaluation of the small bowel and hence a more precise preoperative diagnosis of small bowel tumors. Endoscopic tattooing will help in a minimally invasive (laparoscopic) approach in such patients [31].

It has been reported that small intestinal adenocarcinomas with an adenomatous component had a better 5-year survival than those without an adenomatous component. Also, lymph node metastasis and distal location (jejunum and ileum) were independent predictors for a worse prognosis [10]. For patients who underwent resection, reduced performance status, higher stage, and residual disease after resection predicted overall survival [9]. Another study found that age more than 75 years, lack of surgical resection, higher stage, and duodenal tumors were associated with a poor prognosis. The median survival was 50.1 months with localized disease, 22.2 months with locally advanced disease, and 8.6 months with metastatic disease [32].

A retrospective analysis of small bowel adenocarcinomas found positive surgical margins, extramural venous spread, lymph node metastasis, poor differentiation, depth of invasion, and history of CD to be negative prognostic factors. Age, gender, tumor size, and adjuvant therapy did not affect survival [23].

Adjuvant Therapy

As noted earlier, nonspecific and varied presenting symptoms lead to delays in diagnosis and hence are associated

with a late stage and poor prognosis [9]. In view of the rarity of these tumors, not much data are available regarding the use of adjuvant chemotherapy or radiotherapy. 5-Fluorouracil (5-FU)-based regimens have been used in most series [32]. 5-FU has been combined with platinum-based agents (cisplatin, carboplatin, and oxaliplatin). Those receiving 5-FU combined with a platinum-based agent showed a better response rate and median progression-free survival [33]. Radiotherapy has been combined with chemotherapy in duodenal adenocarcinoma [34]. Another study found no difference in 5-year survival between those who did and did not receive concurrent 5-FU and radiotherapy. But patients with margin-negative resection had 83 % 5-year overall survival compared to 53 % in patients with surgery alone [35].

Conclusion

Small bowel adenocarcinomas are difficult to diagnose because of nonspecific signs and symptoms, delayed presentation, and lack of accurate diagnostic studies. These are usually diagnosed during emergency for acute abdomen with small bowel involvement. If the overall survival of patients with small bowel tumors is to be improved, clinicians must have a high index of suspicion. DBE and wireless capsule endoscopy in patients with obscure gastrointestinal bleeding will help in preoperative diagnosis of jejunal tumors. In such cases a minimal invasive approach to bowel resection may be useful. Adjuvant chemotherapy and radiotherapy have been tried but may not offer much benefit.

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