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Small Bowel Adenocarcinoma: Case series and review from a single Southeast Asian tertiary center

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Abstract

Small Bowel Adenocarcinoma (SBA) is rare despite the small bowel being the longest part of the alimentary tract. SBAs are often diagnosed at late and advanced stages due to atypical symptoms and lack of reliable diagnostic tools. In most instances, SBAs are incidentally detected during laparotomy for acute abdomen. Herein, we report four cases of SBA from a Southeast Asian tertiary center which was collected over five years. In these cases, the discussion on diagnostic and treatment options are reported to arouse clinical awareness and index of suspicion among clinicians and diagnostician alike for early SBA detection.

Keywords

Small bowel; small intestine; adenocarcinoma.

Introduction/Background

Small Bowel Adenocarcinomas (SBA) are not common despite the small bowel being the longest part of the alimentary tract. SBAs are usually diagnosed late and at advanced stages due to atypical clinical symptoms and diagnostic limitations. Cases of SBA are rarely reported in the literature and it is clinically challenging to diagnose. In this case series and mini-review, we report four cases of SBA encountered from the year 2014 till 2019 at Hospital Pulau Pinang, Malaysia, a tertiary center. As the prognosis of SBA remains poor, our objective is to share our experience, create awareness and increase the index of suspicion among clinicians and diagnosticians alike for early SBA detection.

Case Presentation

The first case was a 62 year old male who presented with right iliac fossa pain associated with

abdominal distension. An abdominal X-Ray showed small bowel dilatation while the Contrast-Enhanced Computer Tomography (CECT) similarly confirmed the former with a transition at mid-ileum and possible perforated appendicitis. He also had a raised Carcinoembryonic Antigen (CEA) of 435 ng/mL. He then underwent a laparotomy in which he was found to have intraluminal SBA with invagination of the serosa. Small bowel resection and anastomosis were performed. Histopathology report depicted a moderately differentiated adenocarcinoma with tumor perforation to the visceral peritoneum and lymph node metastasis. Post-operatively, he recovered well and was discharged home. He was planned for chemotherapy which eventually refused. A repeated CECT a month later showed disease progression with liver and lung metastasis. He later presented again with intestinal obstruction and underwent a second laparotomy, segmental bowel resection, and anastomosis for recurrence of SBA. He progressively recovered again and was discharged back home. As the patient persistently refused chemotherapy and any further treatment, he eventually succumbed and passed away due to disease progression.

The second case was a 37 year old male who presented with an abdominal mass and pain. The CECT was consistent with proximal SBA. He underwent laparotomy, end block resection, and a duodenojejunal end-to-end anastomosis, left hemicolectomy, and feeding jejunostomy. Histopathology report depicted a moderately differentiated adenocarcinoma with lymph node metastasis and invading the colon. The resected margins were clear and the patient recovered well after the surgery. However, he subsequently defaulted to follow up.

The third case was a 48 years old lady who presented with epigastric pain and vomiting. An Oesophageal Gastroduodenoscopy (OGDS) showed gastric outlet obstruction. The CECT showed soft tissue thickening in proximal jejunum with proximal bowel obstruction. She then underwent a laparoscopic assisted jejunum tumor resection. Intraoperatively, an SBA of the jejunum was found 10cm from a duodenojejunal junction with proximal jejunum dilatation. The small bowel specimen was reported as well-differentiated adenocarcinoma. She recovered well post-operatively. She completed eight cycles of capecitabine (XELODA) and is currently under the oncology team follow-up. At the time of writing almost four years later, she is well with an Eastern Cooperative Oncology Group (ECOG) Performance Score of 0.

The fourth patient was a 51 years old lady who was initially diagnosed to have ascending colon carcinoma. The CECT scan showed a long segment of circumferential bowel thickening involving the ascending colon causing focal dilatation. Surprisingly, an SBA at the proximal jejunum was found alongside the aforementioned ascending colon tumor during surgery. The patient underwent a laparoscopic right hemicolectomy. Histopathologically, the specimens showed moderately differentiated mucinous adenocarcinoma and well-differentiated adenocarcinoma for the large and small bowels respectively. There were no nodal metastasis and the resected margins were clear. Postoperatively, she developed a surgical site infection but subsequently recovered well and was discharged. She completed eight cycles of Capecitabine plus Oxaliplatin (XELOX) chemotherapy. Currently, she is two years post-surgery with an ECOG Performance Score of 0 and a series of CEA levels below 4.7 ng/mL.

Discussion

SBA is a rare malignancy. An estimated annual global incidence as low as only 2-3 cases are reported per 1,00,000 people [1]. Similarly, the incidence of SBA is relatively low in Malaysia. The Malaysia National Cancer Registry Report 2012-2016 reported a low representation of 0.26% from all tumors reported. It has a slight male predominance of 58% of the total cases [2]. Such occurrence was also reported in other settings around the world [3]. SBA is also 50 folds less common in incidence than colorectal carcinomas (CRC) [4]. Other than that, the most common sites for the SBA are the duodenum followed by the jejunum and ileum respectively [3]. SBA usually occurs during the sixth or seventh decade of life [1]. Surprisingly, we encountered younger patients from the cases we presented. As postulated by Overman, the rarity of SBA may be due to rapid epithelial cell turnover that avoids epigenetic damage, the existence of immune surveillance by the small intestine lymphoid tissues, and an alkaline environment that does not favor carcinogenesis [4]. Additionally, Li et al. postulated that the abundance of Immunoglobulin A (IgA) and rapid transit time in the small bowel when compared to the large intestine, may also play a role in the low carcinogenesis in the small bowel [5].

Inflammatory bowel diseases such are Chron's and celiac diseases are the major causes of SBA. Besides, cancer syndromes such as hereditary nonpolyposis colorectal cancer (HNPC) or Lynch Syndrome, familial adenomatosis polyposis (FAP), Peutz-Jeghers syndrome, multiple endocrine neoplasia syndrome type 1 (MEN1), and neurofibromatosis type 1 are also risk factors for SBA [3,4,6,7].

Unlike CRC, SBA is not widely screened. SBA is difficult to be diagnosed and the diagnosis is often delayed since the small bowel's length, difficulty in capturing intramural masses with scoping, and the lack of reliable and non-invasive tools [8]. However, the diagnosis efficacy of SBA has increased over the years with the availability of push enteroscopy, Video Capsule Endoscopy (VCE), and deep small bowel enteroscopy (DBE) such as the balloon and spiral enteroscopy [8]. As CT and Magnetic Resonance Imaging (MRI) may only detect SBA in the cases of small bowel obstruction, a CT or Magnetic Resonance (MR) enteroclysis and enterography are more sensitive to diagnose SBA. We encountered a similar experience with our first and fourth cases which had a negative CECT finding. The VCE is an excellent tool to diagnose SBA but may be of little use in the case where bleeding and poor bowel preparation are encountered. Furthermore, the VCE technology is of little use when biopsies are needed. This is where the push enteroscopy may be useful to overcome this limitation for both biopsy and bleeding control. On the other hand, the Double-Balloon Enteroscopy (DBE) may reach the anterograde depth of 2 to 3 m and may be convenient for biopsy and preoperative tattooing [6,8]. Interestingly, the sensitivity of endoscopy is poor in several instances such as Chron's Disease, and is not recommended as a surveillance tool for such population [9].

Although the role of adjuvant chemotherapy has not been established for SBA, the treatment can be approached in two ways which are the locoregional and metastatic disease [4,6]. Surgical resection remains the mainstay for the locoregional approach. This is important for the number of lymph nodes that are derived during resection. A microscopically margin negative resection (R0) approach is preferred. For duodenal tumors at the second part of the duodenum or an infiltrating tumor at the proximal or distal duo-

denum, a duodenopancreatectomy resection is indicated [10,11]. Although regional lymph node dissection is performed, extended dissections are not recommended by experts [10]. Segmental duodenal resections are indicated for the first and third parts of the duodenum. As for jejunal and ileal tumors, an R0 with lymph node resection should be performed. An ileocecal resection or right hemicolectomy should be performed if the last ileal loop is involved [10,11]. On the other hand, primary tumor resection is generally not recommended in the metastatic setting except in case of acute bowel obstruction, perforation, or uncontrolled bleeding. In the metastatic setting, surgical resection is not recommended except in the cases of acute bowel obstruction, perforation, or uncontrolled bleeding [7].

To date, there is no randomized study that has evaluated the benefits of systemic chemotherapy in SBA [7]. Regimes such as the 5-fluorouracil/leucovorin plus oxaliplatin (FOLFOX), capecitabine plus oxaliplatin (CAPOX), and oxaliplatin, and capecitabine (CAPIRINOX) has been used as first-line chemotherapy for SBA. We reported the usage of capecitabine in our third patient. The folinic acid, 5FU, and irinotecan (FOLFIRI) regimes have been used for patients in the second-line setting among those who failed the platinum-based therapy [7,11]. In our fourth case, we experienced the usage of XELOX which is also known as CAPOX.

Radiation is usually used alongside chemotherapy when surgical margins are involved. The combination of the aforementioned has also been used to downgrade unresectable SBA [11]. In cases of peritoneal metastases, cytoreductive surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) have been used although further studies are needed to confirm its promising results [11]. When these therapies are contraindicated in patients, the pressurized intraperitoneal aerosol chemotherapy (PIPAC) seems to be a better and futuristic option [11]. Interestingly, immunotherapy targeting the Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGFR) are emerging therapies for SBA [11].

Generally, the prognosis of SBA is poor and a recent study has shown that the median survival time is one year [12]. Proximal location of the SBA, higher Charlsone Deyo Comorbidity Score (CDCC) score, higher grade, and positive lymph nodes were associated with reduced survival [13]. Besides, an ECOG of 3-4, poorly differentiated tumor, low albumin, high Lactic Acid Dehydrogenase (LDH), high CEA, high neutrophil to lymphocyte ratio, and CA 19.9 were among other factors associated with poor prognosis [14]. In a meta-analysis, the overall survival of SBA patients was related to lymph node involvement, margin status, stage, and tumor differentiation [15]. Even though the prognosis of SBA was poor, a Japanese study concluded that combined therapies including local treatment of metastasis may prolong patient survival [14].

Conclusion

In conclusion, SBAs are rarely seen and reported. We reported these cases to arouse clinical suspicion of SBA. The utilization of DBE and VSE may benefit the early detection of small bowel malignancy. Although the exact role of adjuvant chemotherapy and radiotherapy needs further studies, isolated studies have shown the association of better survival and prognosis. There is also a call for the development of future diagnostic means to aid in the early detection of SBA.

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