CASE REPORT

A SUCCESSFUL DOWNSTAGING OF AN IRRESECTABLE DUODENAL ADENOCARCINOMA TO A SUCCESSFUL WHIPPLE'S PROCEDURE, NEVER LOSE HOPE: A CASE REPORT

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Small bowel cancer is a rare cancer that contributes to less than 5% of all gastrointestinal cancers. Whereas primary duodenal adenocarcinomas account for approximately 50% of all small bowel cancers. The annual incidence rate worldwide is less than 1 case per 100,000. The median age of presentation is 67 years. There is no gender predilection. The common histological types include adenocarcinoma, neuroendocrine tumour, Gastrointestinal stromal tumour, and lymphoma.

Keywords: Duodenal adenocarcinoma; Palliative chemotherapy; Unresectable tumour; Surgery

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INTRODUCTION

Small bowel cancer is a rare cancer that contributes to less than 5% of all gastrointestinal cancers. Whereas primary duodenal adenocarcinomas account for approximately 50 % of all small bowel cancers. The annual incidence rate worldwide is less than 1 case per 100,000.[1] The median age of presentation is 67 years.[1] There is no gender predilection. The common histological types include adenocarcinoma, neuroendocrine tumour, Gastrointestinal stromal tumour, and lymphoma. The risk factors include sedentary lifestyle, alcohol, smoking, dietary factors, inflammatory bowel disease, lynch syndrome, Peutz Jegher's disease and familial adenomatous polyposis. Patients often present with nonspecific symptoms leading to delay in diagnosis.[2] The low incidence and the lack of specificity of clinical presentations and complex anatomical position contributes to the diagnostic challenge. Consequently, there is a significant delay in the diagnosis.[2] The diagnostic workup includes a CT chest and abdomen, barium studies and esophagogastroduodenoscopy. However, the diagnosis can be challenging especially if the tumour is in the third or fourth part of the duodenum. Tumour markers like carcinoembryonic antigen and Ca 19.9 can sometimes be helpful in diagnosis and response evaluation and surveillance of these patients. Further tests like microsatellite instability are also important in deciding about the adjuvant chemotherapy options. After completion of diagnostic and staging workup, these patients need discussion in multidisciplinary meeting for assessment of respectability. In advanced and un-resectable disease, the palliative bypass procedures are required. Given its rarity, there is lack of evidence-based data on therapeutic options and biological behaviour. Most of the data comes from retrospective research with a small number of patients treated over decades with diverse treatment techniques. Aggressive upfront surgical resection is considered the most effective and only curative treatment[3], which can be combined with adjuvant chemotherapy. Chemoradiation should be considered in case of positive margins. In clinical practice patients with advanced unresectable duodenal carcinomas, palliative bypass procedures are followed by treatment with palliative approach with guarded prognosis.

CASE REPORT

A 46-year-old male was referred to our hospital with a diagnosis of moderately differentiated adenocarcinoma of the duodenum. He had a history of diffuse abdominal pain, bilious vomiting, severe constipation, and 20 kg weight loss over 6 months. An esophago-gastroduodenoscopy performed at another health facility revealed a mass involving the third and fourth parts of the duodenum. He underwent gastrojejunostomy at another healthcare facility for gastric outlet obstruction. The histopathology from a referred block was reviewed at our hospital which confirmed moderately differentiated adenocarcinoma [Figure-1ab]. The patient was discussed in multidisciplinary team meeting and an upfront Whipple's procedure was planned. Upon a trail of dissection, the tumour was found to be involving superior mesenteric vessels, root of mesentery, mesocolon and attachment to a loop of jejunum, hence was deemed irresectable. The patient was referred to

Medical Oncologist for further management. He received twelve cycles of 5 Fluorouracil/Folinic acid in combination with Oxaliplatin (FOLFOX regimen) till December 2019. The CT scan upon completion of chemotherapy showed stable disease. Therefore, the patient was followed up with serial computed tomography scans and carcinoembryonic antigen levels. During this period the patient remained symptom free, and the scans continued to show stable disease. In April 2021, the patient developed acute cholangitis with jaundice, itching and fever. The CT scan revealed intrahepatic biliary cholestasis along with progressive but potentially resectable peri-ampullary mass with associated peripancreatic lymph nodes. The patient was managed conservatively with supportive care and intravenous antibiotics. Later a percutaneous transhepatic biliary drainage (external) catheter was placed for decompression. The patient recovered in a couple of weeks. In view of clinical remission, good performance status, young age and potential resectability on serial imaging, it was decided to re-explore the surgical options. Therefore, he was referred to the Hepato-Pancreato-Biliary surgeon. His updated imaging in June 2020 was carefully reviewed (Figure-4). Although there was some increase in the bulk of the tumour but there seemed less vascular invasion and hence resectable disease. Hence a repeat trial of surgical resection through Whipple's Surgery was given. Per operatively he was found to have extensive adhesions from previous surgeries requiring over 2 hours of adhesiolysis to identify anatomy. The tumour was extending to involve the mesocolon, right gonadal vessels and ureter was adherent but separate from the tumour. It was a complex surgical procedure because of two previous surgical explorations including a bypass procedure. However, a successful Whipple's procedure with negative margins was performed. Because of complex anatomy due to three surgical procedures in total, the patient's post operative course was complicated by gastric outlet obstruction. A CT Abdomen and pelvis showed marked gastric dilatation with oral contrast. No flow of contrast seen from gastrojejunostomy site. Thereafter he underwent Oesophago gastro duodenoscopy which showed that the distal stomach was closed with a blind end. The gastrojejunostomy was present in the proximal stomach, without any structuring to cause mechanical obstruction. He was managed conservatively with supportive care and Naso-jejunal tube feeding and rehabilitation. The patient showed slow but gradual clinical improvement, his oral intake improved slowly and gradually and he started gaining weight. After recovery from the post operative sequels the patient was reevaluated in medical oncology clinic with repeat imaging and histopathology results. His post operative CT chest abdomen showed post operative changes and his histopathology revealed pT3N2 moderately differentiated adenocarcinoma, involving four out of nineteen lymph nodes. In view of significant residual disease on histopathology he was given adjuvant chemotherapy with FOLFOX for six months. The patient remains on surveillance through follow up computed tomography scans and tumour markers every three to four months. As of his last visit in February 2023, patient remains disease free.

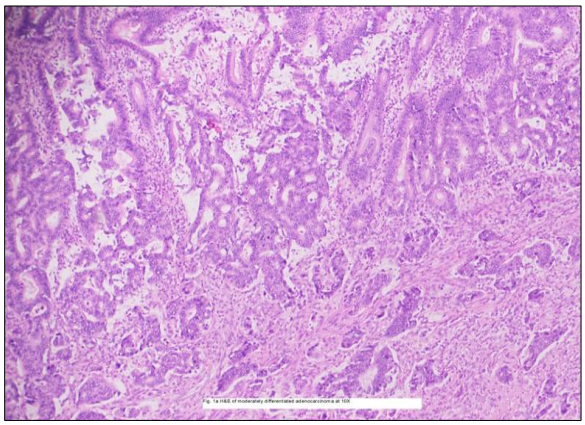

Figure-1a H&E of moderately differentiated adenocarcinoma at 10X

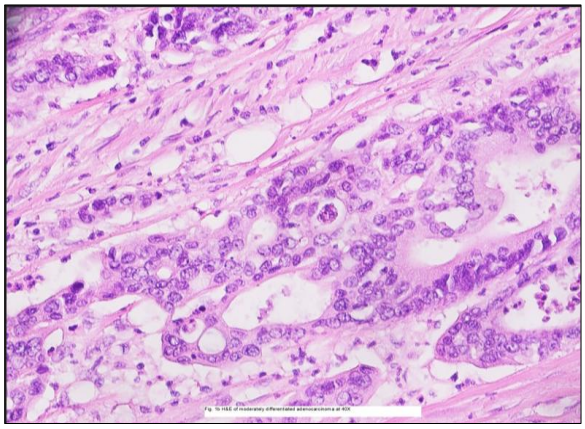

Figure-1b H&E of moderately differentiated adenocarcinoma at 40X

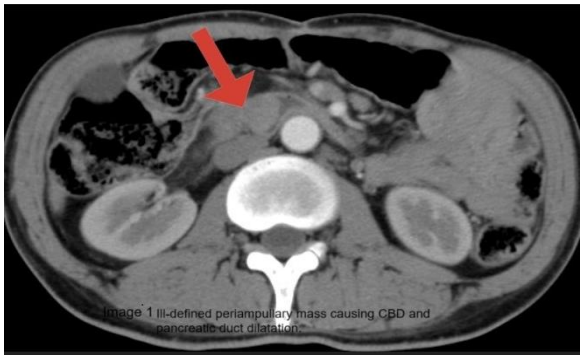

Figure-3: An image illustrating an Ill-defined periampullary mass causing CBD and pancreatic duct dilatation.

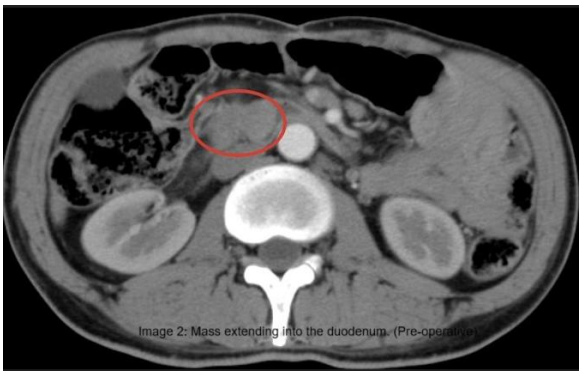

Figure-4: Image showing mass extending into the duodenum. (Pre-operative).

DISCUSSION

This case report represents a rare form of gastrointestinal tumour with an unusual clinical course. The initial work up of the patient was performed at another medical facility where he was diagnosed with the primary duodenal carcinoma and a bypass procedure was performed because of advanced unresectable disease. Although the tumour was discernable on the imaging, the tumour could not be visualized at the time of the initial endoscopy at our center because of complex post bypass anatomy. The diagnosis and management of the primary duodenal adenocarcinoma can sometimes be very challenging. 1–15% Primary duodenal adenocarcinoma is located in the first, 50–75% in the second, 14–33% in the third, and 5–17% in the fourth part of the duodenum.[4–6] Unfortunately, many patients with duodenal adenocarcinomas have nonspecific symptoms and poorly defined natural history, they are usually diagnosed at an advanced stage. The symptoms can be very vague sometimes.[6] There is an average delay of 2–15 months from the onset of symptoms to the time of diagnosis of primary duodenal carcinoma.[7] Upper gastrointestinal endoscopy screening cannot pick up the disease within the horizontal and ascending portions. Examining the entire duodenum using upper gastrointestinal endoscopy is challenging; Adenocarcinomas of the 3rd and 4th portions of the duodenum are frequently inaccessible using endoscopy, and most cases require multiple investigations.[8] Although the patient was initially assessed for surgery at our hospital, the curative intent surgery was aborted because of advanced disease due to proximity to the vital vascular structures. Thereafter, the patient was referred for palliative chemotherapy, which he received uneventfully. Since two efforts at surgical resection had failed, therefore the patient was kept on surveillance. In patients with resectable disease, pancreaticoduodenectomy remains the preferred surgical option for adenocarcinoma of the first and second part of the duodenum and segmental resection is often reserved for adenocarcinoma of the third and fourth part.[4] However, majority of patients are diagnosed at an advanced stage when the possibility of curative resection is almost non-existent. Tumours deemed irresectable and subjected to systemic chemotherapy usually do not maintain sustained response. Paradoxically this patient showed stable disease for a long period of time. Therefore, down the line when the serial scans continued to show stable disease, further surgical options were re explored. And excitingly this effort at surgery was a success story. Nevertheless, because of two prior surgical explorations this time the procedure was not a straightforward one. There were extensive adhesions and the surgeon had to spend significant time on the adhesiolysis. By the end of the day the surgical team was able to resect the tumour with negative margins.

The important aspect of management in this case was looking for curative options even after the initial treatment with palliative intent. The disease stability over a period of 14–16 months reflected good biological behavior and less chances of distant metastasis. Therefore, the patient was given the best chance for cure with resection.As we are aware, duodenal carcinomas are rare tumours. Hence till recently clinical trials and guidelines were not available for the management of these tumours. In the management of these patient most of the data is extrapolated form the guidelines on periampullary and colon cancer. Recently only, French and National Comprehensive cancer Network (NCCN) guidelines were developed with best evidence of category 2A. In these guidelines most of the data is extrapolated from the trials carried out on other gastrointestinal carcinomas such as colon. According to NCCN guidelines the patients treated successfully with surgery needs 6 months of adjuvant 5-FU based chemotherapy. Since this patient had significant residual disease on histopathology therefore, he was treated in adjuvant setting with 6 months of 5FU based chemotherapy. There is an ongoing phase II Ballad trial on the role of adjuvant chemotherapy in small bowel cancer. Once the results are evaluated, we will be able to better define the treatment guidelines and clinical practices further.

CONCLUSION

In conclusion we present a case report with the theme of keeping the horizons open for complex patients. As medical oncologists, we would individualize the care for our patients, evaluating the variable biological behaviours of diverse tumours with the same pathology. Such biological behaviour and response highlight the need for genetic testing, Next Generation Sequencing and a more personalized approach in the

management of these patients. As an ever-emerging field, we hope for further studies and more personalized management protocols.

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