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Case Report

Duodenal Metastasis from Colorectal Cancer: A Case Report

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Abstract

Background: The occurrence of metastatic colon lesions in various organs has been documented extensively in the literature. The liver, lungs, and bones are the most frequently affected sites. Metastasis in the duodenum due to colon cancer is an infrequent occurrence. ***Case Presentation:*** We present a detailed case report of a 65-year-old female patient diagnosed with metastatic colon cancer to the duodenum. The patient initially underwent extended right hemicolectomy for stage III low-grade adenocarcinoma of the colon. Adjuvant chemotherapy was administered, resulting in a period of apparent remission. However, in 2020, the patient experienced elevated tumor marker levels, prompting further investigations. Endoscopy revealed an irregular mass infiltrating the muscle layer in the duodenum, confirming malignant involvement. The patient underwent curative distal gastric duodenectomy, with pathology results indicating a colonic origin of the tumor. The patient received first-line palliative chemotherapy with FOLFOX rechallenge and the addition of AVASTIN. Several cycles of chemotherapy were completed, with satisfactory tumor response observed in follow-up PET scans. Maintenance therapy was initiated after achieving disease-free status on CT scans. However, in October 2022, the patient exhibited increasing tumor marker levels and new findings on PET scan, leading to the initiation of second-line palliative therapy with FOLFIRI and ramucirumab. The patient has received multiple cycles of second-line therapy, with the most recent PET scan in February 2023 showing a favorable treatment response, including a decrease in the size of existing nodes and no identification of new lesions. ***Conclusion:*** In conclusion, this case exemplifies the journey of a patient with stage 3 colon cancer who initially responded well to surgery and adjuvant chemotherapy, but experienced subsequent relapse in the duodenum. Despite surgical intervention and palliative chemotherapy, the patient developed metastasis in the liver, lung, and multiple lymph nodes.

Keywords: colon cancer, metastasis, duodenum, adjuvant chemotherapy, palliative chemotherapy.

INTRODUCTION

Colorectal cancer is the third most common cancer worldwide. It is the third most common cancer in men and the second most common cancer in women [1]. More than 90 percent of colorectal carcinomas are adenocarcinomas originating from epithelial cells of the colorectal mucosa [2]. The most common sites of metastasis are the liver and the peritoneum [3]. New treatments for primary and metastatic colorectal cancer have been developed and include laparoscopic surgery for primary disease; resection of metastatic disease affecting, for example, the liver and lungs; radiotherapy for rectal cancer and some forms of metastatic disease; and neoadjuvant and palliative chemotherapy [4]. Other new treatments include targeted therapy, where the major types of targeted drugs are monoclonal antibodies and small molecule inhibitors [5]. Such drugs are advantageous because, unlike chemotherapy, they can be chosen based on the molecular characteristics of tumor types [6]. However, a large number of patients experience disease progression even after receiving standard regimens [7]. In the future, personalized medicine, in which drugs and drug combinations are optimized based on each patient's available data including their genetic and epigenetic features and alterations, will improve the

efficacy of treatments, reduce side effects, and benefit cancer patients [8]. Furthermore, metastatic lesions to the small bowel are more common than primary lesions and most common primary neoplasms that metastasize to the duodenum are lung cancer, renal cell carcinoma, breast cancer, and malignant melanoma [9]. This case report describes a patient diagnosed with stage 3 colon cancer that developed into stage 4 colon cancer metastatic to duodenum and other visceral organs.

CASE REPORT

A 65-year-old woman sought medical attention at Burjeel Hospital due to gastrointestinal symptoms. Upon examination, she was diagnosed with mild gastritis. However, during a colonoscopy, a tumor was discovered in the cecum. Subsequent biopsies confirmed the presence of malignancy in the tumor. The patient travelled to NUH Hospital in Singapore and underwent an extended right hemicolectomy on September 24, 2017. The pathology showed moderately differentiated low-grade adenocarcinoma of the colon, PT4N1 M0, Stage III. Patient subsequently returned to UAE and was recommended to start adjuvant chemotherapy for a period of six months starting 31/10/2017. She completed six cycles of FOLFOX adjuvant chemotherapy on 30/4/2018, with some delays due to frequent neutropenia requiring G-CSF growth factor stimulation. On June 22, 2018, CT chest, abdomen, and pelvis was performed for restaging and to assess the bone window of right shoulder due to arthritis, which showed abnormal bone texture and a bone scan was advised to rule out bone metastasis. Therefore, a bone scan was conducted on August 12, 2018, which detected a small focal increase activity in the mid third of the left femur that could be due to a stress fracture and metastasis cannot be excluded. Furthermore, a Positron Emission Tomography (PET) scan was done on the 1st of October 2018, which confirmed the benign nature of the bony lesion and showed no FDG avid findings suggestive of recurrent or metastatic malignant disease. Meanwhile the patient was following up in the clinic and her labs were improving, with adequate counts and tumor marker CEA and CA 19-9 were both within normal. She underwent a mammogram on April 22, 2019, which showed no evidence of focal suspicious lesions.

During her follow-ups in August 2019, a CT scan chest, abdomen and pelvis was requested and she was referred to the gastroenterology clinic for the first surveillance colonoscopy, which was reported to be normal with no signs of recurrence. The CT scan showed no significant cervical, mediastinal, or intra-abdominal lymph nodes and no acute changes in comparison to previous imaging. Her abdomen and pelvis CT showed no signs of metastasis. On December 9, 2019, the patient was seen in the oncology clinic and her labs showed borderline neutropenia and hypercalcemia, but recent tumor markers CEA and CA 19-9 were both within normal range. Based on the labs, she was advised to stop calcium replacement and to increase hydration and to follow-up in six weeks for a scheduled follow up and heparin flushing of port-a-cath. On June 28, 2020, the patient was seen in the clinic and was referred to the interventional radiology clinic for removal of port-a-cath as she had completed two years post-treatment. Her next scheduled appointment was after two months. Later, on November 7, 2020, the patient had rising CEA tumor markers so a PET scan was done for clinic correlation, which showed an FDG-avid lesion in the gastric antrum/pylorus and FDG-avid subpyloric nodes, which were suspicious for metachronous malignancy, and heterogenous sclerotic changes throughout the axial skeleton without abnormal FDG uptake, of uncertain significance, which was query for hematologic disorders or metabolic bone disease. An endoscopy was recommended based on these findings.

The patient was referred to a gastroenterology clinic for an endoscopy as well as a colonoscopy. An Esophago-Gastro-Duodenoscopy (EGD) was done on November 19, 2020, which showed antral gastritis, clean base ulcer 3mm just before the pyloric opening, which was biopsied. The biopsy showed features consistent with chemical gastritis, and no H. Pylori were identified on Warthin Starry stain. She was seen in the gastroenterology clinic on December 2, 2020 and the recommendations included starting the patient on PPI for the gastric ulcer and scheduling a repeat EGD to confirm the was ulcer healing, as well as a colonoscopy. Following that, a repeat EGD was done on January 5, 2021, which showed no ulcer in the stomach, hypertrophied fold in antrum with normal mucosa. Flat, friable infiltration seen in D1, easily bleeding, biopsies were obtained that showed superficial villiform tissue fragments with high-grade dysplastic change. A colonoscopy was also done on the same day. It showed a rectal polyp, which was biopsied. Otherwise, the rest of the colon was normal to the anastomosis site. The rectal biopsy showed benign hyperplastic polyp.

The patient was admitted under gastroenterology after two weeks for further assessment of duodenal lesion using endoscopic ultrasound. The results showed D1 posterior wall irregular mass invading the muscle layer in keeping with a malignant lesion. Later on, biopsy results showed fragments of small bowel mucosa with high-grade dysplasia and foci highly suspicious of adenocarcinoma and the patient's daughter was informed about these results. This case was discussed in the tumor board on February 2, 2021. The multidisciplinary team decided to go for surgical resection with curative intent. A distal gastrectomy with gastro-duodenostomy was scheduled on the February 10, 2021. The patient was improving and was discharged after four days. On the February 17, 2021, she visited the emergency department with complaints

of abdominal pain, vomiting, and melena. She developed tachycardia and hypotension and was admitted under general surgery. She received IV fluids and was transfused 1 unit of PRBC. Full septic screen was sent, and she was started on Tazocin. Imaging during admission showed patent anastomosis and no signs of active bleeding.

Furthermore, the patient's distal gastric duodenectomy pathology report showed metastatic moderately differentiated adenocarcinoma of colorectal origin present in adventitia and invading small bowel wall with 3 out of 8 lymph nodes also positive for metastatic carcinoma with focal extranodal extension [3/8]. No serosal involvement seen. No lymphovascular space or perineural invasion was identified. Immunohistochemistry subsequently performed on the current tumor showed the tumor cells are CK7-/CK20+, which is consistent with origin from a previous colonic primary. This favored the metastatic origin from colon primary rather than primary duodenal cancer, which is M1 disease. Afterwards, the patient was seen in the oncology clinic and referred to interventional radiology for port-a-cath insertion. She was scheduled on March 14, 2021 to be started on FOLFOX rechallenge first line palliative chemotherapy in addition to targeted therapy depending on the result of molecular studies including RAS and BRAF results. She was also prescribed Neupogen injections after pump removal.

On the March, 28th 2021, the patient's regimen was altered based on KRAS mutation and immunotherapy, AVASTIN was added to the third cycle FOLFOX rechallenge 1st line palliative chemotherapy, however due to dysfunction of the port-a-cath, the session was cancelled and rescheduled after the port-a-cath replacement. Furthermore, on April 27th, 2021, the immunohistochemistry for HER-2 was inconclusive. FISH was ordered and is pending. DNA mismatch repair testing showed no loss of nuclear expression of MMR proteins: no evidence of deficient mismatch repair (low probability of MSI-H). PDL1: Combined Positive Score (CPS) was 5 KRAS - MUTANT. NRAS Wild. BRAF Wild. Throughout her treatment, on June 21, 2021, the patient developed a mild allergic reaction to oxaliplatin with hives all over her body. Oxaliplatin was stopped and hydrocortisone and diphenhydramine were given. The patient only received Avastin and infusional 5 FU. And the plan was to suspend oxaliplatin and bolus 5FU from all future cycles.

The patient received seven cycles of oxaliplatin, the last was on July 5, 2021, and 5FU bolus was omitted on Cycle 8. Overall, she completed 12 doses of 5FU and Avastin rechallenge on September 27, 2021. A CT scan chest abdomen and pelvis was requested on November 7, 2021 for re-evaluation, which showed no evidence of disease recurrence or metastatic disease in chest abdomen and pelvis, so the patient was switched to treatment every three weeks. The patient had persistent neutropenia despite modification of drug doses and duration. She wasn't showing any clinical symptoms after completing six months of maintenance therapy. There was also no evidence of disease on the latest CT scan in March, therefore the primary physician decided to stop the maintenance therapy with a plan to follow up on the patient in four months with labs and a CT scan every six months for the next two years, along with referring her to the gastroenterology clinic for upper and lower endoscopy for follow up in two months. The last dose of maintenance was received on March 18th, 2021.

The patient also had small and large joint pain, mainly in the left shoulder with limited movement for two weeks, for which she was referred to rheumatology and managed accordingly. The follow-up upper endoscopy done on July 10, 2022 reported an ulceration at site of duodenal surgery, which was biopsied. The colonoscopy reported the presence of hemorrhoids and diverticula. Biopsy was obtained and the pathology report concluded there was no evidence of colitis or malignancy and no evidence of Helicobacter pylori organism. The patient was seen in the clinic on October 11, 2022. Her full labs were okay while the tumor markers showed significant increase. CEA level from 3 to 21 and CA 19-9 level from 14 to 51. A CT scan performed reported progressive disease with bilateral new small lung nodules in addition to three new liver lesions. She was referred for PET scan on November 16, 2022, which reported disease progression with new FDG-avid liver and lung metastases. New FDG-avid mediastinal, internal mammary, upper abdominal, and retroperitoneal nodal metastases. On November 21, 2022, she was switched to second-line palliative therapy with FOLFIRI and ramucirumab and the possibility of liver lesion ablation was discussed with IR physician. She received total of six cycles and was to be re-evaluated with a PET scan on February 9, 2023, which showed favourable treatment response as compared to November 2022 with decrease in size and FDG avidity of mediastinal, internal mammary and retroperitoneal nodes. Few FDG-avid nodes persist, representing mild residual disease. Near-complete resolution of FDG-avid liver lesions. Lung nodules were grossly stable. A few decreased mildly in size. Most were unchanged. No new FDG-avid lesion was identified. So far, the patient has received 11 cycles of FOLFIRI and ramucirumab and is scheduled for a re-evaluation PET scan.

DISCUSSION

Most colon cancers are classified as adenocarcinomas, subdivided according to the grade of the tumor into low-grade and high-grade [10]. The genomic analysis of colon cancer provides data on the presence of activating mutations in the *KRAS,*

NRAS and *BRAF*, thus providing criteria for the selection of patients for the anti-epidermal growth factor receptor (EGFR), Cetuximab or Panitumumab [11]. Mutations in these genes are mutually exclusive and occur globally in about 55–60 percent of colorectal cancers [12]. Patients with *KRAS*, *NRAS* or *BRAF* mutations do not benefit from anti-EGFR therapies. In addition to providing predictive and prognostic information, multigene sequencing for the molecular profiling of colorectal cancer will provide data to discriminate between microsatellite stability (MSS) and MSI. MSI-high (MSI-H) colorectal cancers result from mutations in mismatch repair (MMR) genes that cause a multifunctioning gene product or from promoter methylation causing the epigenetic silencing of MMR protein expression (MMR-deficient). MSI-H or MMR-deficient colorectal cancers may have alternative therapeutic options based on the administration of some immunological agents [13]. Recurrence of colorectal cancer is seen in about 30-40 percent of patients who undergo primary curative surgical resection and it usually recurs in the first two years after surgery [8].

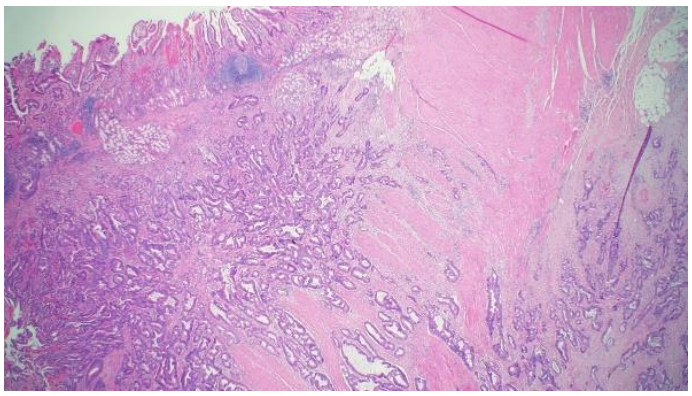

Figure 1: H&E stained microphotograph, low power magnification X4. Upper part showing duodenal mucosa with submucosal Brunner glands, underlying tumor infiltrate involving submucosa, muscularis propria, and subserosa

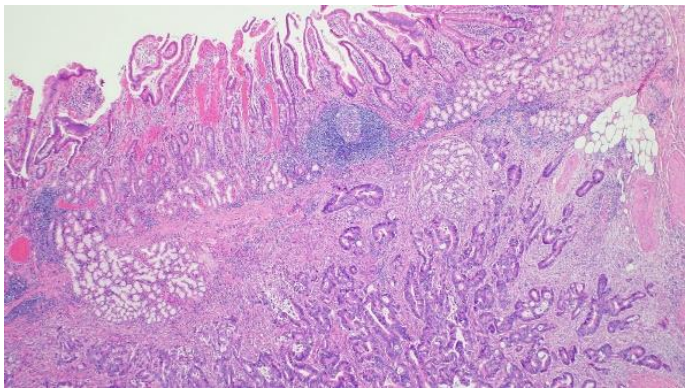

Figure 2: H&E stained microphotograph, magnification X10. Upper part showing duodenal mucosa with submucosal Brunner glands, underlying tumor infiltrate involving submucosa, muscularis propria, and subserosa

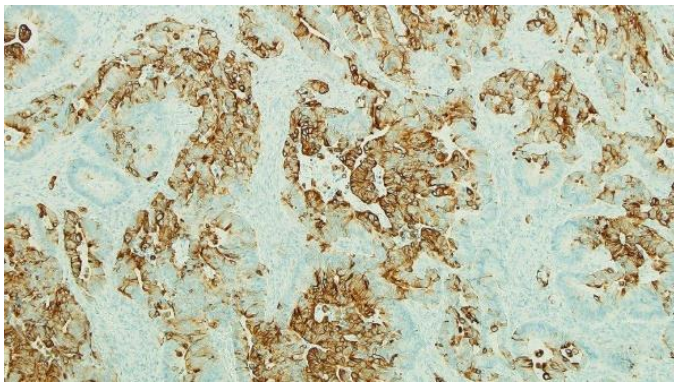

Figure 3: Immunostaining shows tumor cells are positive with CK20 consistent with intestinal phenotype

The most common sites of metastasis from colon cancer are the regional lymph nodes, liver, lung, and the peritoneum [14]. It is extremely rare to have right-sided colonic tumors causing delayed metastatic involvement of the duodenum after resection of the primary tumor. Although very rare, cases of colon cancer with duodenal metastasis have been described in the literature along with the pathogenesis of metastasis to the duodenum [15]. Lymphatics from the right colon drain to the periduodenal lymph nodes leading to lymphatic spread from the colon to the duodenum. Also, the mesentery of the hepatic flexure of the colon lies in direct contact with the second portion of the duodenum, forming a pathway for metastatic spread by way of lymphatics [16]. Direct extension from the colon to the duodenum is also possible, but it's less likely. Various primary neoplasms have their own distinct way of metastasis to duodenum, such as metastasis from lung, breast, and melanoma spreads via blood and lymphatics while metastasis from colon, ovary, and stomach spreads via peritoneal involvement [17].

As the number of colon cancer survivors increase, it is expected that the incidence of metastasis to uncommon sites will increase as well [18]. According to the report published by the Surveillance, Epidemiology and End Results (SEER) Program, patients with five or more years of survival after the diagnosis of small intestine cancer were found to have a two-fold increase in risk of colon cancer. Similarly, patients with colon cancer were also found to have increased risk of small intestine cancer and these risks were amplified in patients whose primary cancer was diagnosed before 60 years of age [18]. To help differentiate the origin of the tumors, immunohistochemistry (IHC) is usually done. Colorectal adenocarcinoma has typical IHC markers of CK7 (–) and CK20 (+), while small intestine tumors have CK7 (+) and CK20 (–) [19]. In our case, the patient's tumor cells were CK7-/CK20+, which was consistent with origin from a previous colonic primary. According to the guidelines, systemic chemotherapy regimens including FOLFOX, FOLFIRI, bevacizumab, and/or other targeted therapies are recommended for stage IV disease [20]. The use of bevacizumab has significant benefits in metastatic colorectal cancers, treatment patterns may evolve such that more patients with metastatic colorectal cancer can access prolonged treatment with bevacizumab in maintenance regimens or in treatment beyond progression [21].

CONCLUSION

In conclusion, the case exemplifies the journey of a patient with stage 3 colon cancer who initially responded well to surgery and adjuvant chemotherapy but experienced subsequent relapse in the duodenum. Despite surgical intervention and palliative chemotherapy, the patient developed metastasis in the liver, lung, and multiple lymph nodes. This case report also demonstrates the diagnostic challenges faced in identifying a malignant tumor in the cecum of a 65-year-old woman presenting with mild gastritis, emphasizing the importance of thorough investigations and biopsies to confirm malignancy.

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

Ethical approval

As per international standard or university standard, written ethical approval has been collected and preserved by the author(s).

Competing Interests

Authors have declared that no competing interests exist.

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