Multiple Primary Malignancies of the Colon, Stomach, and Kidney in a Patient with Bowel Obstruction Requiring Emergency Surgery: A Case Report

Kholoud H. AlBaqmi
Faisal A. AlMudaiheem
Sami Boghdady
Khadijah A. AlHussaini
Nada Shokor
Nourah AlOudah

Conflict of interest: None declared

Source of support: King Abdullah International Medical Research Center, Ministry of National Guard – Health Affairs, Riyadh, Saudi Arabia

Patient: Male, 63-year-old
Final Diagnosis: Colon adenocarcinoma
Symptoms: Abdominal pain • constipation
Medication: —
Clinical Procedure: —
Specialty: Surgery

Objective: Rare co-existence of disease or pathology

Background: Multiple primary malignancy (MPM) is defined as 2 or more primary malignancies diagnosed in the same patient. Even though MPMs are rare, various associated tumors have been reported in the literature. We report the first case of triple synchronous primary malignancies: gastrointestinal stromal tumor, colon adenocarcinoma, and renal cell carcinoma.

Case Report: A 63-year-old man presented to our emergency department with a 7-day history of diffuse abdominal pain and constipation. Examination revealed a distended abdomen and diffuse tenderness. Enhanced computed tomography showed a high-grade large bowel obstruction with the transitional zone seen at the splenic flexure, which was suspicious for primary colon cancer, and a hypodense lesion on the left mid-pole of the kidney. An emergency exploratory laparotomy revealed a splenic flexure mass, which was resected, and a left renal mass, which was excised. A stomach mass at the greater curvature was an incidental intraoperative finding; a wedge resection was performed for it. The pathology for each of the masses showed a primary malignancy.

Conclusions: Multiple primary cancers are rare and a multidisciplinary team approach is essential for management of these patients, be it preoperative, intraoperative, postoperative, or long-term surveillance.

MeSH Keywords: Carcinoma, Renal Cell • Colorectal Neoplasms • Gastrointestinal Stromal Tumors

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/926472
Background

Multiple primary malignancy (MPM) was first reported in the 1900s by Billroth [1] and the definition then was redefined by Warren and Gates [2] as the existence of 2 or more primary malignancies in the same patient. The tumors can be synchronous or metachronous. The North American Association of Central Cancer Registries defines synchronous tumors as those identified less than 6 months apart; tumors diagnosed more than 6 months apart are known as metachronous. Here we describe the case of a 63-year-old man who presented with adenocarcinoma of the colon, gastrointestinal stromal cell tumor (GIST), and renal cell carcinoma (RCC). To our knowledge, this the first reported case in the English literature of synchronous tumors of the colorectum, GIST, and RCC.

Case Report

A 63-year-old man with hypertension who had never undergone surgery presented to our emergency department with a 7-day history of diffuse abdominal pain and constipation. He had smoked a pack of cigarettes a day for the past 45 years. He had no personal or family history of malignancy. Physical examination revealed a distended abdomen and diffuse abdominal tenderness. The results of initial laboratory tests were unremarkable. The patient’s carcinoembryonic antigen level was 4 ng/mL and his cancer antigen 19-9 level was 12 U/mL. Enhanced computed tomography showed a high-grade large-bowel obstruction with a transitional zone at the splenic flexure, which was suspicious for primary colorectal cancer (CRC) (Figure 1). Two lesions also were seen in the left kidney. A 2.6×2.7×2.7-cm well-rounded, hypodense lesion with high attenuation (66 HU) was present in the mid-pole, and another small 1.5×1.4-cm exophytic cystic lesion with fluid attenuation was present in the lower pole of the left kidney (Figure 2). There were 2 indeterminate small, hypodense lesions in segments 8 and 6 of the liver (Figure 3). No other abdominal masses initially were identified. Renal ultrasonography performed the same day to assess the kidney masses showed a complex cystic lesion in the mid-pole of the left kidney and another simple, exophytic, cortical cyst measuring 1.2 cm (Figure 2).

The patient underwent an urgent exploratory laparotomy, which revealed a splenic flexure mass; it was resected and a primary anastomosis was performed. A partial nephrectomy also was performed for the left renal masses. During intraoperative inspection, a mass was found at the greater curvature of the stomach. It measured approximately 3×3 cm and was hard, round, and had a smooth surface. We elected to do a wedge resection of the stomach to excise the mass.

The pathological evaluation of the colon specimen showed a 4.5×4×1.5-cm, moderately differentiated, invasive adenocarcinoma. The tumor was invading through the muscularis propria into the subserosal adipose tissue and the non-peritonealized pericolic/perirectal soft tissues but did not extend to the serosal surface; there was no regional lymph node metastasis (pT3N0Mx) (Figure 4). No KRAS, NRAS, nor BRAF mutations were identified, nor was there a loss of nuclear expression of MSI/MMR proteins. The left mid-pole kidney lesion was a papillary RCC, Type 1, WHO/ISUP grade I, 3.3 cm in the greatest dimension, with no lymphovascular invasion (pT1aNxMx) (Figure 5). The patient was found to have a mutation in the PDGFRA gene, which is a member of the type III receptor tyrosine kinase family. The lower-pole lesion was found to be a 1.4-cm papillary, cortical adenoma with cystic changes. The stomach lesion was found to be a GIST, mixed subtype: spindle and epithelioid (pT2NxMx). It was 2.8 cm in greatest

Figure 1. (A–C) Selected sagittal (A) and Axial (B) computed tomography scans of the upper abdomen with intravenous contrast in the portosystemic venous phase and oral contrast in our patient, who presented with suspected bowel obstruction. The images show focal circumferential narrowing of the descending colon at the splenic flexure, resulting in an “apple core” appearance that is pathognomonic for colonic adenocarcinoma (green arrow) and leads to high-grade bowel obstruction.
dimension, with moderate lymphocytic infiltrate (Figure 6). The
tumor was low-grade (1/50 HPF) and had no malignant fea-
tures, which, along with its size, carried a 1.9% risk for pro-
gressive disease [3].

A chest computed tomography (CT) scan performed 4 days
after surgery showed bilateral, small, likely benign subpleu-
rnal nodules and a mixed sclerotic/lytic right 9th rib lesion.
Furthermore, magnetic resonance imaging of the liver, per-
formed 1 month postoperatively to evaluate the liver mass-
es, revealed a segment 4A lesion measuring 2×1.7 cm, which
was definitely a metastatic lesion from the colon adenocarci-
noma, and another benign small cyst in segment 5 (Figure 7).
Because the patient had been taken to surgery urgently to
relieve his obstruction, his case was discussed at a postoper-
ative tumor board meeting. The plan was to further investi-
gate his liver lesions, to start him on concurrent chemothera-
py, and to repeat the CT images in 3 months.

Discussion

MPMs are considered rare and they typically have been de-
scribed in case reports [4,5] and in reports from registries and
centers in different countries [6,7]. The mechanism of develop-
ment of MPMs is uncertain and likely multifactorial; identified
risk factors include previous cancer treatment, diet, smoking,
and genetic mutations [8]. Smoking alone is a significant risk
for cancer [9], and, together with alcohol intake, has been estimated to account for approximately 35% of all excess risk for MPMs [8]. Most secondary primary tumors have been found to occur in tobacco-related cancer sites, particularly in other digestive organs. This may be due to the similar carcinogenic agents that affect the gastrointestinal system [10,11]. With advances in healthcare systems around the world and the increase in different modalities for diagnosis and management, the life expectancy of the population has increased significantly in the past few decades, according to the World Health Organization [12]. Given the increasing incidence of MPM, individuals who are elderly are at increased risk of developing them [13]. A retrospective study of more than 52,000 patients by Bittorf et al. [6] showed that 2.8% had 3 primary malignancies. Interestingly, the 5-year survival rate for patients with MPMs has been shown to be higher than for those who have solitary malignancies. The reason for that remains unclear. There are multiple reports in the literature of associated synchronous MPMs. For instance, patients diagnosed with CRC are at a higher risk for RCC than those in the general population, and vice versa [14]. It has been suggested that both neoplasms

Figure 4. (A) Gross image of the left splenic flexure colonic mass. The mass is ulcerated and measures 4.5×4.0×1.5 cm. A low-magnification microscopic image of the colonic mass (moderately differentiated colonic adenocarcinoma). There are infiltrating, atypical glands with desmoplastic reaction. (B) The tumor extends into the pericolic adipose tissue. A higher-magnification microscopic image of the colonic mass. (C) Extensive surface erosion with inflammatory exudate also is present, which suggests ulceration. Unremarkable colonic mucosa (arrow) is adjacent to the infiltrative tumor cells. (D) The tumor is composed of infiltrating, atypical glands with large nuclei and focal luminal necrosis along with a desmoplastic reaction, consistent with moderately differentiated colonic adenocarcinoma.
are associated with genetic predisposition and share a common pathogenic mechanism [14–18]. Synchronous tumors are believed to originate from tissues and organs with a similar embryonic origin [14, 19]. This association frequently has been reported with CRC [14].

GIST is another example. It was reported to be associated with different malignant tumors, including RCCs [19–22]. Furthermore, it is known to be part of multiple syndromes, including the Carney triad, Carney-Stratakis syndrome, and neurofibromatosis type 1 (NF1).

**Conclusions**

The present report describes the first case of MPM of the colon, stomach, and kidney. The diagnoses were made based on the patient’s history, physical examination, and imaging.

Given the broad spectrum of causes for developing MPM, as have been previously discussed, physicians should be attentive to the possibility of new or separate primary malignancies. A high index of suspicion is warranted based on patient history, including age, predisposing risk factors, and family history. Physical examination and different imaging modalities can be employed even if a primary malignancy has been definitively diagnosed.
Figure 6. (A) Microscopic image of the gastrointestinal stromal tumor (GIST). The tumor is composed of subepithelial interlacing spindle cell proliferation. Genetic testing of the tumor confirmed a PDGFRA gene alteration with wild-type KIT. (B) Higher-magnification microscopic image of the low-grade (G1) GIST. The tumor is composed of interlacing, essentially spindle cell proliferation with dilated vessels. No necrosis is evident. The tumor has 1 mitosis per 50 high-power fields, and thus, very low risk/low malignant potential. (C) Microscopic image of immunostaining of the GIST. The strong positivity for DOG-1 underscores the mesenchymal origin of the tumor.

Figure 7. (A) Follow-up T2-weighted magnetic resonance image with fat saturation and (B) Post contrast T1-weighted image with fat saturation 1 month later demonstrate high T2 signal intensity and peripheral enhancement of the lesion, respectively, in keeping with metastasis from the colonic adenocarcinoma.

To date, no management guidelines have been established for MPMs. Therefore, the approach to treatment, screening, and follow-up should be tailored to each individual patient, ideally by a multidisciplinary team.
References:

1. National Cancer Institute: SEER Program Code Manual. 3rd ed. Bethesda (MD): The Institute; 1998, https://seer.cancer.gov/manuals/codeman.pdf
2. Warren S, Gates O: Multiple primary malignant tumors: A survey of the literature and a statistical study. Am J Cancer, 1932; 16: 1358–414
3. Foo WC, Liegl-Atzwanger B, Lazar AJ: Pathology of gastrointestinal stromal tumors. Clin Med Insights Pathol, 2012; 5: 23–33
4. Angurana SL, Kapoor R, Kumar P et al: Quadruple malignancy in a single patient: A case report and comprehensive review of literature. J Cancer Res Ther, 2010; 6: 230–32
5. Demandante CG, Troyer DA, Miles TP: Multiple primary malignant neoplasms: Case report and a comprehensive review of the literature. Am J Clin Oncol, 2003; 26: 79–83
6. Bittorf B, Kessler H, Merkel S et al: Multiple primary malignancies: An epidemiological and pedigree analysis of 57 patients with at least three tumours. Eur J Surg Oncol, 2001; 27: 302–13
7. Coleman MP: Multiple primary malignant neoplasms in England and Wales, 1971–1981. Yale J Biol Med, 1986; 59: 517–31
8. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health: The health consequences of smoking – 50 years of progress: A report of the surgeon general. Atlanta (GA): Centers for Disease Control and Prevention (US); 2014
9. Curtis RE, Freedman DM, Ron E et al. (eds.), New malignancies among cancer survivors: SEER cancer registries, 1973–2000. National Cancer Institute, NIH Publ. No. 05-5302. Bethesda, MD, 2006. https://seer.cancer.gov/archive/publications/mpmono/
10. Mysuru Shivanna L, Urooj A: A review on dietary and non-dietary risk factors associated with gastrointestinal cancer. J Gastrointest Cancer, 2016; 47: 247–54
11. Ahnet CC: Carcinogenic food contaminants. Cancer Invest, 2007; 25: 189–96
12. World Health Organization: World Health Statistics 2019: Monitoring Health for the SDGs, Sustainable Development Goals. Geneva: World Health Organization, 2019. https://www.who.int/gho/publications/world_health_statistics/2019/en/
13. Wood ME, Vogel V, Ng A et al: Second malignant neoplasms: Assessment and strategies for risk reduction. J Clin Oncol, 2012; 30: 3734–45
14. Calderwood AH, Huo D, Rubin DT: Association between colorectal cancer and urologic cancers. Arch Intern Med, 2008; 168(9): 1003–9
15. Steinhagen E, Moore HG, Lee-Kong SA et al: Patients with colorectal and renal cell carcinoma diagnoses appear to be at risk for additional malignancies. Clin Colorectal Cancer, 2013; 12(1): 23–27
16. Amoroso A, Porto FD, Garzia P et al: The infrequent association of synchronous renal and colonic malignancies. Eur Rev Med Pharmacol Sci, 1999; 3(3): 111–14
17. Bhargava A, O'Callaghan M, Abdelhafiz T et al: Synchronous sigmoid and caecal cancers together with a primary renal cell carcinoma. Ir J Med Sci, 2012; 181(2): 273–76
18. Dafashy TJ, Ghaffary CK, Kayes K, Sonstein J: Synchronous renal cell carcinoma and gastrointestinal malignancies. Case Rep Urol, 2016; 2016: 7329463
19. Papalampros AE, Petrou AS, Mantonakis EI et al: Coexistence of a colon carcinoma with two distinct renal cell carcinomas: A case report. J Med Case Rep, 2011; 5: 134
20. Wen J, Li H, Gang Ji Z et al: Simultaneous renal clear cell carcinoma and gastrointestinal stromal tumor in one case. Urol Ann, 2013; 5(2): 122–23
21. Dasanu C, Jethava A, Ali S, Codreanu I: Gastrointestinal stromal tumor of small intestine and synchronous bilateral papillary renal cell carcinoma. Conn Med, 2013; 77(7): 405–7
22. Torous V, Su A, Lu D, Dry S: Adult patient with synchronous gastrointestinal stromal tumor and Xp11 translocation-associated renal cell carcinoma: A unique case presentation with discussion and review of literature. Case Rep Urol, 2015; 2015: 814809

AlBaqmi K.H. et al.: Case report of multiple primary malignancies of the colon, stomach, and kidney © Am J Case Rep, 2020; 21: e926472

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]