Synchronous adenocarcinoma of colon and urothelial carcinoma: case report

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ABSTRACT
Synchronous renal and colon malignancies is a recognized clinical entity with low incidence. The relationship between these two cancers remains unclear, but various genetic and environmental factors have been implicated in the pathogenesis. A 52-year-old Filipino female with a palpable supraumbilical mass underwent a series of examinations, which revealed a transverse colon mass, and an incidental finding of a right renal mass. We did an extended right hemicolectomy and right radical nephrectomy, with an uneventful postoperative course. Histopathologic examinations revealed colonic adenocarcinoma and urothelial cell carcinoma of the right renal pelvis. Future plans for the patient include providing adjuvant chemotherapy using the Mayo regimen and performing ureterectomy with bladder cuff. The diagnosis of two distinct primaries was only established through postoperative histopathology results, which resulted in a delayed definitive management of the urothelial cell carcinoma. A frozen section biopsy, which is not routinely done for the surgical management of renal masses, would have contributed to an accurate intraoperative diagnosis and a more immediate and appropriate management of the urologic malignancy.

Keywords: multiple primary malignancies, surgery, oncology, frozen section biopsy, urologic malignancy, colon malignancy

INTRODUCTION
Multiple primary malignancies (MPM) was first described by Billroth at the end of the 19th century.1 MPM is considered when: each of the tumors represents a definite pattern of malignant disease; each malignancy is distinct; and the possibility of one tumor being a metastasis of the other has been excluded.2 Synchronous malignant tumors are diagnosed simultaneously or within an interval of six months.3 We report a case of a patient with synchronous malignancies of the transverse colon and the renal pelvis.

CLINICAL FEATURES
A 52 year-old female was admitted in our hospital with a chief complaint of abdominal mass. She had episodes of hematochezia for two years, with no previous consultations nor medical intervention. Four months prior to admission, she noticed an approximately 2 x 2 cm supraumbilical mass that gradually increased in size, associated with epigastric and periumbilical pain and weight loss, which prompted her to seek consultation.

The patient had no history of vomiting, obstipation, dysuria, hematuria, or flank pains. Her past medical and family history were unremarkable. She denied any history of smoking, alcoholic beverage drinking, drug abuse, or exposure to toxic chemicals. Physical examination revealed pale palpebral conjunctivae, and flabby, soft and non-tender abdomen. We were able to palpate a hard, mobile, non-tender, irregular 4 x 4 cm mass in the supraumbilical area.

DIAGNOSTIC APPROACHES
We requested for multiple hematologic and biochemical tests, which only revealed anemia (hemoglobin 8.4 g/dL). A barium enema was initially done, revealing a narrowing in the transverse colon, measuring 5.6 cm in length, with an apple-core appearance. We requested an abdominal CT scan, which showed an enhancing mass measuring 5.9 x 3.1 cm in the transverse colon, with multiple enhancing nodular densities in the transverse mesentery. The scan further revealed a well-
defined, lobulated enhancing mass in the middle and inferior segments of the right kidney, with internal calcification measuring 4 x 3.9 x 4.4 cm (Figure 1). The patient’s urinalysis results revealed microscopic hematuria and bacteriuria. The other diagnostic work-ups that we did, including chest X-ray, and carcinoembryogenic antigen (CEA) and alkaline phosphatase levels, were all within normal limits.

We corrected the anemia of the patient by transfusing 600 mL of packed red blood cells. Hemoglobin post-transfusion was 10.1 g/dL. The patient underwent an extended right hemicolectomy and right radical nephrectomy.

The biopsy specimen from the hemicolectomy (Figure 2) was composed of a portion of the terminal ileum, cecum with the appendix, ascending colon, and part of the transverse colon, with pericolic fat and the mesentery. Grossly, the intestines measured 28 x 12.3 x 7 cm. The mass measured 5 x 5.6 cm, and it occupied more than 50% of the largest diameter of the intestine. There were 42 lymph nodes isolated, with the largest measuring 1.3 cm. Based on the intraoperative findings, we staged the transverse colon mass as a IIA carcinoma.

On the other hand, the specimen from the nephrectomy (Figure 3) was composed of the right renal tissue measuring 9.6 x 5.0 x 5.5 cm, with intact capsule, perinephric tissue, and an attached ureter. The specimen’s cut section revealed a tan, soft, cauliflower-like mass attached in the pelvis and major calyces, measuring 6 cm in greatest dimension. Based on the intraoperative findings, we diagnosed the renal mass as a Stage II carcinoma.

The patient was discharged 5 days after the surgical procedures and had an unremarkable post-operative course. Histopathologic findings were released a week after surgery. The intestinal specimen showed that all lines of resection were devoid of tumor cells (Figure 4). The 42 isolated lymph nodes were all negative for tumor cells. However, tumor cell invasion was noted in the lymphatic and perineural vessels, except for the blood vessels. These findings were consistent with colon adenocarcinoma stage IIA (pT3N0M0).

Sections from the renal mass revealed fused, branching, and delicate papillae that
were lined by anaplastic transitional cells with slightly pleomorphic nuclei (Figure 5). There was invasion to the lymphatic vessels. The blood vessels and ureter were free of tumor cells. The histopathological findings led to a diagnosis of urothelial cell carcinoma of the right renal pelvis stage III (T3N0M0).

The surgical and histopathologic findings (Table 1) were vital to the definitive diagnosis for this patient’s condition. Given the two distinct histopathologic results, we considered the patient as having synchronous adenocarcinoma of the colon and urothelial cell carcinoma. The patient was advised by the colorectal team to start adjuvant chemotherapy using the Mayo regimen six weeks after her surgery. Chemotherapy is ongoing as of this report. On the other hand, the urology team plans to carry out a complete oncologic resection of the urothelial cell carcinoma, hence the patient was also advised to undergo right ureterectomy with bladder cuff post-chemotherapy.

**DISCUSSION**

The association of colorectal carcinoma and renal tumors has been previously described, with incidence of 0.3% to 4.85%. Among patients with urologic cancer, MPM exists in 3.3% to 10.3%. This is the first documented case in our institution.

The exact mechanisms involved in the occurrence of MPM are not yet fully elucidated. DNA mismatch repair and overexpression of tumor suppressor genes have been proposed as possible mechanisms. Risk factors for the development of this condition include strong family history of cancer, Lynch II syndrome, and environmental factors such as tobacco, pollution, exposure to asbestos, petroleum products, heavy metals, ultraviolet light, therapeutic chemotherapy, and radiotherapy. Our patient did not have any of the risk factors mentioned.

Management of concomitant colonic and kidney malignant masses involves simultaneous radical resection of both malignancies in one surgical session. The usual approach is by open laparotomy, but laparoscopic resections have also been done. For complete oncologic resection of the tumor, nephroureterectomy is recommended for urothelial cell carcinoma of the upper urinary tract in a patient with a normal functioning contralateral kidney. Since
Figure 4 High-power field view (x1000) of the colonic mass tissue showing irregular glandular structures (orange ring) invading the underlying lamina propria. These glands are lined by atypical columnar cells exhibiting increased nuclear-to-cytoplasmic ratio, moderate nuclear pleomorphism, nuclear hyperchromatism, and prominent nucleoli. There were areas showing moderate nuclear stratification (orange ring) of up to four cell layers, and majority of the atypical nuclei (yellow ring) had rounded to oval shape. There was a moderate degree of mononuclear inflammation among the tumor cells.

Figure 5 Microscopic views (A: x40, B: x100) of the renal mass tissue (B: upper left quadrant) showing fused, branching, and delicate papillae (A: red ring).

Our patient did not present with symptoms leading to a clinical suspicion of urothelial cell carcinoma, we initially managed her as having an incidental renal cell carcinoma, and we only did a radical nephrectomy. Histopathologic reports are crucial in establishing whether one of two concomitant tumors is metastatic from the other or both tumors are primary.\(^9\) In our patient, we have ruled out metastatic neoplasms postoperatively, based on the different histopathologic characteristics of the two tumors. Upon confirmation of the urothelial cell carcinoma diagnosis, we advised our patient to undergo ureterectomy with bladder cuff after adjuvant chemotherapy.

Adjuvant chemotherapy is recommended for stage IIA colorectal carcinoma to decrease recurrence rate rather than prolong survival.\(^{14}\) Although controversial if used in stage II colon cancer patients,\(^{15}\) adjuvant systemic chemotherapy improves survival for high-risk patients.\(^{16}\) The recommended follow-up post-operative diagnostics include monitoring of CEA level every three to six months for two years, then every six months for a total of five years; chest, abdominal, and pelvic CT scan annually for up to five years; and colonoscopy one year after resection.\(^{14}\)

As in our patient’s case, a stage II colonic adenocarcinoma has a 5-year recurrence rate of 10%\(^{17}\) and an observed 5-year survival rate of 66.7%,\(^{18}\) while stage III urothelial carcinoma has a lower five-year survival rate of 16-33%.\(^{8,14}\) In one study, patients with localized renal cancer with different coexisting cancers had poorer overall survival compared to those with localized renal carcinoma alone.\(^3\)

**CONCLUSION**

A patient presented to us with a palpable abdominal mass, CT scan findings of a colonic mass, and an incidental finding of a right renal mass, hence we did an extended right hemicolectomy and a right radical
nephrectomy in one setting. Post-operative biopsy results revealed a stage II A colon adenocarcinoma and a stage III urothelial carcinoma. A frozen section biopsy, which is not routinely done for the surgical management of renal masses, could have helped us early on in coming up with a more accurate intraoperative diagnosis. A suspicion of a urothelial cell carcinoma would have provided a good reason for considering a right nephroureterectomy with bladder cuff at the outset.

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REFERENCES