Management of colon-invading renal cell carcinoma: Operative technique and systematic review

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INTRODUCTION

At detection, 5%–15% of renal cell carcinomas (RCCs) invade into the surrounding structures.[1,2] Extracapsular spread may involve psoas muscle, pancreas, spleen, small bowel, and colon.[3–5] Synchronous metastases commonly coexist and preclude surgical intervention. Overall, locally advanced disease confers a poor prognosis, with 5-year overall survival rates of <5%.[6,7] Nonetheless, en bloc resection of involved organs remains the only potentially curative option.

Direct colonic invasion by RCC is rare.[8,9] Here, we perform a systematic review of the literature to identify previously reported cases of colon-invading RCC. We also outline the operative approach for a recently encountered case of right-sided, colon-invading RCC.

METHODS

Literature search
A systematic review was conducted according to the Preferred Reporting Items for Systematic Review and
Meta‑Analysis (PRISMA) guidelines. A study protocol has not been previously published.

Eligibility criteria
All published reports of primary colon-invading RCC were eligible for inclusion. Case reports, case series, and cohort studies were eligible for inclusion. Conference abstracts were excluded. Eligible studies reported on clinicopathological characteristics, postoperative outcomes, and survival data, where available.

Study outcomes
From the included studies, two reviewers extracted the following details: tumor size, laterality, structures invaded, staging, histopathological features, immunohistochemical features, and surgical management.

Search strategy
Online databases were searched using the following combination of Medical Subject Heading terms: “renal cell carcinoma” OR “RCC” AND “colon.” PubMed, EMBASE, and Scopus databases were searched. The search was performed from inception until May 2020, with the last search performed on May 1, 2020. The titles and abstracts of citations were individually reviewed, and full texts of studies were retrieved, where available. Articles not in the English language were excluded. Reference bibliographies of the recovered studies were further assessed for potential additional publications suitable for inclusion.

Intraoperative photography and chart review
A chart review was performed on a patient who presented with right‑sided colon‑invading RCC. The following details were extracted: clinicopathological characteristics, radiological images, intraoperative photographs, histopathological images, operative technique, and postoperative outcomes. Informed written consent was obtained from the patient.

RESULTS
Study selection and characteristics
Figure 1 shows the PRISMA flowchart of our search strategy. The initial search captured 2464 results. After screening, 59 full‑text articles were assessed for eligibility. From these, four case reports were identified. One case was identified locally. Following a chart review, five cases of locally advanced T4 RCC invading the colon were included [Table 1].

Details of previously reported cases
Paine et al.[11] reported the case of a 53‑year‑old male presenting with intermittent hematochezia and left flank pain. Initial computed tomography (CT) scanning showed a 7‑cm left renal mass that was visualized at colonoscopy in the left colon, with fistulous communication present. Biopsy at the time of endoscopy confirmed a poorly differentiated carcinoma, with absence of glandular and squamous features. The authors performed a left radical nephrectomy and partial colectomy with formation of a transverse colostomy. Histopathological evaluation of the specimen showed a mass arising in the renal capsule and invading the adherent colon. Details on postoperative outcomes were not reported.

Wu et al.[12] reported the case of a 42‑year‑old male who presented with leg edema, shortness of breath, and weight loss. Due to renal failure, the patient underwent hemodialysis. CT scanning demonstrated a large (28 cm), right‑sided renal tumor. Invasion into the caudate lobe of the liver, as well as into the right retroperitoneal structures and the hepatic flexure of the colon, was present. The diagnosis of RCC was confirmed by percutaneous biopsy, which also showed sarcomatoid differentiation. The patient underwent nonoperative management. Survival outcomes were not reported.

Pompa and Carethers[13] reported a left‑sided case of RCC presenting with occult gastrointestinal hemorrhage. CT scanning demonstrated a large (110 mm × 80 mm × 65 mm), left‑sided RCC. The mass, in the left lower quadrant, involved the left kidney and descending colon, with extension into the associated adrenal gland and spleen. Biopsy showed a spindle cell RCC, with sarcomatoid
differentiated present. Operative management or patient outcomes were not available.

Perez et al.\(^{[14]}\) reported a case of left-sided RCC present with lower gastrointestinal hemorrhage. CT scanning showed a left-sided T4 RCC that invaded the left sigmoid colon. This was the first reported case to use colonoscopy-aided biopsy to confirm the diagnosis. Histopathological evaluation showed a clear cell RCC with sarcomatoid differentiation. The authors performed a left radical nephrectomy and left hemicolectomy.

**Description of newly reported case**

A 68-year-old Caucasian male presented with large-volume melena and collapse. He was hypotensive (80/40 mmHg) on initial assessment and was responsive to fluid resuscitation. Hemoglobin was measured at 11.5 g/dL. There was no history of preceding bowel symptoms, hematuria, or flank pain. Six months previously, he underwent coronary artery stenting and was taking dual antiplatelet therapy. Interestingly, he had a fraternal twin brother who had a nephrectomy for malignancy. A complete urological examination and baseline laboratory investigations were otherwise normal.

A CT scan was performed following identification of the renal mass at focused assessment with sonography for trauma scan. Initial imaging identified a heterogeneously enhancing solid mass in the mid-pole of the right kidney \([6.5 \text{ cm} \times 4.3 \text{ cm} \times 5.4 \text{ cm}; \text{Figure 2}]\). The tumor extended anteriorly through the Gerota's fascia to involve the posterior aspect of the right colon. There were numerous sub-centimeter paracolic lymph nodes identified on cross-sectional images. However, there was no tumor thrombus seen within the right renal vein, and there was a single right renal artery. Overall, radiological evaluation suggested locally advanced, nonmetastatic RCC. Endoscopic evaluation of the mass showed an exophytic, invasive mass visualized on the posterior intraluminal aspect of the hepatic flexure of the colon [Figure 3a]. Histopathological evaluation of colonic biopsy confirmed RCC. Following discussion at a multidisciplinary meeting, the patient was planned for simultaneous open extended right hemicolectomy and radical right-sided nephrectomy.

**Gross pathological evaluation** showed a 5.1 cm × 3.8 cm × 7.5 cm hemorrhagic tumor mass extending through the Gerota's fascia and into the posterior aspect of the right colon. Histopathological appearances confirmed a RCC (clear cell type; ISUP Grade 4) with sarcomatoid differentiation [Figure 3b-d]. Nineteen pericolic nodes were retrieved and were histologically negative for metastatic disease. Final TNM staging was pT4N0M0. The surgical margins were negative. The immunohistochemical profile of the tumor was positive for epithelial membrane antigen, vimentin, and CD10.

On the first postoperative day, he required inotropic support and blood transfusion with two units of packed red blood cells. Ten days postoperatively, the patient developed an ileus. A CT scan showed a small collection (9.8 cm × 8.4 cm) which was amenable to conservative management. He was discharged 15 days following his operation. The patient remains well six months postoperatively with no evidence of recurrence.

**Details of operative approach**

A transperitoneal approach was used. Access was obtained using a reverse L-shaped incision. This incision extended from the xiphisternum to the umbilicus and then laterally to the right flank. This enabled optimal exposure of right-sided intraperitoneal viscera and retroperitoneal structures.

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Mobilization of colic and mesocolic components was performed first, followed by mobilization and en bloc resection of the adherent right kidney [Figure 4]. A lateral-to-medial approach was used for mesocolic

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**Table 1: Clinicopathological features of reported cases of primary renal cell carcinomas invading into the colon**

| Authors            | Year | Tumor size (mm) | Side | Invading | Stage | Sarcomatoid | Pathology | IHC                      | Management                        |
|--------------------|------|-----------------|------|----------|-------|-------------|-----------|--------------------------|-----------------------------------|
| Byrnes et al.      | 2020 | 51×38×75*       | Right| Right    | pT4   | Yes         | Clear cell RCC | EMA+, vimentin+ CD10+ Keratin+, vimentin+ S100 | Radical nephrectomy and extended right hemicolectomy Left radical nephrectomy and partial colectomy |
| Paine et al.\(^{[11]}\) | 2012 | 112×105×55*     | Left | Left     | pT4   | Yes         | Clear cell RCC |                               | Left radical nephrectomy            |
| Wu et al.\(^{[12]}\) | 2007 | 200×180         | Right| Liver, colon, adrenal | pT4   | Yes         | RCC, unspecified | Spindle cell RCC |                | Nonoperative                        |
| Pompa and Carethers\(^{[13]}\) | 2002 | 110×80×65**     | Left | Left colon, spleen | pT4   | Yes         | Clear cell RCC |                               |                                    |
| Perez et al.\(^{[14]}\) | 1998 | -               | Left | Sigmoid   | pT4   | Yes         | Clear cell RCC |                               | Left radical nephrectomy and left hemicolectomy |

*Size from gross pathology specimen, **Size measured by CT. IHC: Immunohistochemical profile, Ki-67 LI: Rabbit anti-human Ki-67 antigen labeling index. EMA: Epithelial membrane antigen, -: Unreported data, RCC: Renal cell carcinoma
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Mobilization, beginning inferior to the tumor. The right paracolic peritoneal reflection was divided and extended caudad, toward the inferior margin of the right colon. A plane along the Toldt’s fascia was further developed using a combination of sharp and blunt dissection. Mobilization was performed cephalad until the inferior margin of the adherent tumor was identified. Separation of the mesofascial plane was extended to the root of the superior mesenteric artery and a high vascular ligation was performed. Ligation of the ileocolic, right colic, and middle colic arteries was performed using nonabsorbable sutures and a LigaSure device (Covidien, Dublin, Ireland). The terminal ileum was divided 10 cm proximal to the ileocecal valve using a linear stapling device. Attention was then turned to mobilization of the colon superior to the tumor. The mid-point of the transverse colon was identified and divided using a linear cutting stapler. Following this, the gastrocolic component of the greater omentum was divided laterally from the line of resection using a LigaSure device.

Mobilization of the colic and mesocolic components enabled their retraction and identification of the underlying structures. These structures included the right renal hilum, duodenum, and inferior vena cava. Dissection of perinephric fat enabled complete mobilization of the right kidney. The kidney and adherent hepatic flexure were retracted inferiorly and anteriorly, enabling access to the posterior aspect of the right renal hilum. Double ligation and sharp division of renal hilar vessels was performed in an artery-first manner using nonabsorbable sutures.

Figure 2: Radiological appearance of renal cell carcinoma invading anteriorly into the right colon. (a-c) Images of axial, coronal, and parasagittal sections from corticomedullary phase of contrast study. Renal cell carcinoma outlined in red dotted line. (d-f) Images of axial, coronal, and parasagittal sections from nephrogenic phase study. Renal cell carcinoma outlined in red, adherent colon in blue, and kidney in green.

Figure 3: Endoscopic and histopathological appearance of renal cell carcinoma. (a) Photograph taken at colonoscopy demonstrating intraluminal appearance of renal cell carcinoma. (b) Photograph of the postoperative pathological specimen. Axial section at the level of mid-pole of the right kidney demonstrating direct invasion to the right colon. (c) Photomicrograph of axial histopathological section showing severe nephrosclerosis indicated by dense lymphocytic interstitial infiltrate (red asterisk) and glomerulosclerosis. Red arrow indicates a 400 μm deposit of clear cell renal cell carcinoma (ISUP grade 4). (d) Photomicrograph of axial histopathological section of the colon showing preserved colonic mucosa (red arrow) with complete effacement of the submucosa and muscularis mucosa by clear cell renal cell carcinoma (area below red interrupted line).
The gonadal vessels and ureter were ligated, enabling en bloc excision of the specimen. A side-to-side ileocolic anastomosis was performed using a linear cutting stapler. Both the terminal ends were sufficiently mobilized to ensure a tension-free and well-vascularized anastomosis.

**DISCUSSION**

RCC spread occurs lymphatically, hematogenously, transcoelomically, or by direct invasion. Locally aggressive variants are rare. Given the anatomic proximity of the duodenum, numerous authors have reported direct invasion into the duodenal bulb and ampulla. Gastrointestinal tract invasion may manifest clinically with gastrointestinal hemorrhage or intussusception. However, as the colon and kidney are anatomically remote, direct invasion into the colon is exceptionally rare. A systematic review of the literature found four reported cases of primary RCC invading into the colon [Table 1]. We also present on the reported case successfully managed with open right radical nephrectomy and extended right hemicolectomy:

Colon-invading RCC typically expresses aggressive histopathological features such as sarcomatoid differentiation. Of the five cases, sarcomatoid differentiation was present in all. Conversely, sarcomatoid differentiation is typically present in <5% of clear cell carcinomas. Sarcomatoid RCC (sRCC) is characterized by pleomorphic spindle cells and giant cells, producing a sarcoma-like appearance. Due to the locally invasive nature and metastatic potential of sRCC, it heralds a poor prognosis.

Radical resection of locally advanced tumors is both challenging and controversial. Clinical trials in oncology are conducted on the principle that tumor invasion to the surrounding structures renders the patient “inoperable.” No randomized controlled trials are reported on nonmetastatic RCC invading into the adjacent organs. However, large-volume centers, including Memorial Sloan-Kettering Cancer Centre (MSKCC) and MD Anderson Cancer Centre (MDACC), have reported retrospective data on radical resection for locally advanced disease (pT3/T4). With a median follow-up of 13 months, MSKCC patients incurred a 76% recurrence rate and 90% mortality rate (n = 36). Meanwhile, MDACC reported 83% recurrence rate at a median follow-up of 32 months (n = 30). Radical resection does not confer substantive survival benefit. Patients undergoing radical resection therefore need careful counseling on the overall prognosis and risks of surgery.

Despite a lack of data supporting radical resection in terms of overall survival, there is a clear role of en bloc resection in locally advanced disease. With prudent patient selection, improvements in symptoms, quality of life, and palliation are achievable therapeutic goals. Furthermore, pathological involvement of adjacent organs cannot be predicted by preoperative investigations. For example, reactive desmoplasia seen in large RCCs may obliterate fascial planes and mimic pT4 disease. Tumors are more likely to produce a mass effect through Gerota’s fascia rather than infiltrate it. In locally advanced disease, Margulis et al. suggested that 60% of patients are downstaged on histopathological evaluation of specimens. In the case reported here, we justified radical resection with curative intent on the absence of metastatic disease, the patient’s fitness for surgery, and imminent risk of gastrointestinal hemorrhage.

Careful patient selection relies on anatomical, surgical, and patient factors. Anatomical factors for optimal resection include adequate resection of perinephric adipose tissue, ipsilateral adrenal gland resection, regional lymphadectomy, and an oncologically clear resection of the involved
We opted to perform complete mesocolic excision to achieve an oncologically clear resection, given clinically detectable metastasis disease in the right mesocolon. Failure to obtain a microscopically margin-negative resection is associated with disease progression. For this reason alone, it is important to perform an optimal oncological resection for all the involved structures.

The above factors necessary for optimal oncologic outcomes preclude most patients from resection. However, in patients suitable for radical resection, patient-related factors, such as Eastern Cooperative Oncology Group performance status, lactate dehydrogenase level, serum hemoglobin level, and corrected serum calcium, may aid in the prediction of postoperative morbidity and oncologic outcomes.

Overall, local invasion into the adjacent organs without metastases accounts for <1% of RCC patients suitable for resection. Currently, no data exist to guide the surgical approach. Laparoscopic and robotic approaches likely have elevated rates of complications due to prolonged anesthesia times. Moreover, laparoscopic management of large tumors is technically demanding. Therefore, an open approach is preferred for locally advanced disease in most cases.

Radical resection for locally advanced disease requires careful patient selection and counseling. Simultaneous resection of invaded structures with curative intent is feasible in select patients and can confer added benefits including symptomatic control and improved quality of life. The optimal management of these patients remains unclear. Now that large randomized controlled trials demonstrate the efficacy of targeted therapies including sorafenib and sunitinib in disseminated disease, it remains unclear if surgical intervention and systemic medical therapies can be successfully integrated in select patients.

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Conflicts of interest
There are no conflicts of interest.

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