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Case report

Primary squamous cell carcinoma of the kidney parenchyma with ascending colon invasion: A case report and literature review

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ABSTRACT

Introduction: Primary squamous cell carcinoma (SCC) of the kidney parenchyma is extremely rare, with only seven cases reported to date. Herein, we present a case of primary with colon invasion.

Presentation of case: A 61-year-old man presented right flank pain for 5 months. Computed tomography (CT) showed multiple renal stones and a necrotic mass in the lower pole of the right kidney, which was suspicious for ascending colon invasion. There was no history of radiation or occupational exposure to chemicals. Radical nephrectomy, right hemicolectomy, and lymph node dissection were performed. The kidneys showed a solid mass with multiple renal stones. The tumor comprised nests of atypical squamous cells and keratin pearls; however, the renal pelvis was normal. 18-Fluorodeoxyglucose-positron emission tomography/CT failed to demonstrate other primary site. Therefore, the patient was diagnosed as primary SCC of the kidney. The patient did not receive adjuvant therapy and was alive during follow-up for 6 months after surgery.

Discussion: SCC of the urinary tract is considered to be the result of squamous metaplasia of the urothelium, which may potentially progress to SCC. Squamous metaplasia may be caused by chronic irritation. However, the mechanism of SCC remains unclear. Although the prognosis of SCC is similar to that of urothelial carcinoma when compared stage for stage, SCC tends to be diagnosed at a more advanced stage.

Conclusion: This is a rare case of kidney SCC with adjacent organ invasion. Additional studies are required to further our understanding of this rare tumor and improve diagnosis and treatment.

1. Introduction

Primary squamous cell carcinoma (SCC) of the renal pelvis is a rare but relatively known disease entity, accounting for 0.5%–0.8% of malignant renal neoplasms [1]. Risk factors include renal stones, infection, endogenous and exogenous chemicals, hormonal imbalance, and vitamin A deficiency [2]. In comparison, primary SCC of the kidney parenchyma is extremely rare, with only seven cases reported to date [3–9]. Most cases presented with advanced stage disease, showing extrarenal invasion (Table 1). Here, we report a very aggressive form of primary SCC of the kidney parenchyma. To the best of our knowledge, this is the first report of direct tumor invasion to adjacent organs.

This work has been reported according to the SCARE criteria [10].

2. Presentation of case

A 61-year-old man was referred to our hospital with a 5-month history of dull and intermittent pain in the right flank. He also had a history of weight loss of 6 kg during the last 10 days. Computed tomography (CT) revealed multiple staghorn stones in both kidneys, and the patient was referred to the urology department of our institute for further evaluation. There was no history of gross hematuria and physical examination revealed mild tenderness in the right flank. The patient was a current smoker with a 38 pack-year history and regularly consumed alcohol (15 times a month for 40 years). There was no history of radiation exposure or occupational exposure to any other chemicals. He denied having symptoms such as fever, chills, nausea, vomiting and melena. On admission, his routine blood test results revealed a white blood cell count of 9.56×10^9/L (normal, 4.0–10.0 $\times 10^9$/L), red blood cell count of 3.80×10^{12}/L (normal, 4.23–5.98 $\times 10^{12}$/L), hemoglobin

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of 11.6 g/dL (normal, 13.0–17.0 g/dL), and hematocrit of 35.4% (normal, 38.0–52.0%). C-reactive protein (CRP) was slightly elevated (2.90 mg/dL; normal ~0.30 mg/dL). Renal function test results were also normal, which were albumin of 3.9 g/dL (normal, 3.5–5.2 g/dL), blood urea nitrogen of 15.2 mg/dL (normal, 8.0–23.0 mg/dL), creatinine of 1.01 mg/dL (normal, 0.7–1.2 mg/dL), and glomerular filtration rate of 120 mL/min (normal, 90–100 mL/min). Routine urinalysis showed occult blood (6–10/high power field (HPF)) and leukocytes (31–50 cells/HPF) with no bacteriuria. Of note, hepatitis B antigen was detected for the first time through preoperative evaluation. Other laboratory test results were normal. X-ray of the kidneys, ureters, and bladder (KUB) showed bilateral renal stones and staghorn stones (Fig. 1a). Contrast-enhanced CT showed a necrotic mass in the lower pole of the right kidney, measuring approximately 8.0 cm in diameter. The lesion was suspected to have invaded the perirenal fat (Fig. 1b) and ascending colon (Fig. 1c and d), and para-aortic lymph node enlargement was identified. Based on radiological features, a malignant tumor of renal origin, such as renal cell carcinoma, was highly suspected.

Laparoscopic radical nephrectomy, right hemicolectomy, and lymph node dissection were performed. Grossly, the hepatic flexure of the ascending colon was adhered to the lower pole of the right kidney (Fig. 2a). A relatively well-demarcated, yellow-white solid mass was identified in the lower pole. Multiple staghorn stones observed on KUB filled the pelvicalyceal system and resulted in severe hydronephrosis and thinning of the renal cortex (Fig. 2b). Grossly, the tumor appeared to penetrate Gerota's fascia and invade the ascending colon (Fig. 2c). Microscopic examination revealed well-differentiated SCC composed of large nests of atypical squamous cells, keratin pearls, and desmoplastic stroma with entrapped glomeruli and tubules (Fig. 3a and b). The periphery of the tumor showed chronic inflammatory infiltration. Although extensive sampling of the pelvicalyceal system, there was no evidence of tumor involvement to renal pelvis and also no evidence of squamous metaplasia or urothelial neoplasm, including carcinoma in situ (CIS) (Fig. 3c and d). Therefore, SCC of the renal pelvis was ruled out. Immunohistochemistry showed positivity for cytokeratin 5/6 and p63 and negativity for cytokeratin 20 and GATA3 (Fig. 3e and f). Despite the aggressiveness of the tumor, there was no metastasis to the lymph nodes. Finally, the pathological stage of pT4N0 was assigned. The patient was discharged 10 days after surgery without any complications. 18-Fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT failed to demonstrate any other primary site of SCC. The patient refused adjuvant chemotherapy.

One month later, the patient presented to the emergency room with dysuria and abdominal pain for one week. CT showed an abscess at the surgical site, with no radiological evidence of local recurrence (Fig. 4a). He was hospitalized and treated with antibiotics; his symptoms improved, and CRP decreased, and he was discharged. The patient represented to the emergency room 1 month after discharge with severe abdominal pain. CT revealed a reduction in the size of the known abscess, however mechanical small bowel obstruction, probably owing to adhesions, was identified (Fig. 4b). Laparoscopic adhesiolysis with biopsy was performed to correct the adhesion and rule out tumor recurrence. Histologically, there was no definite evidence of tumor recurrence. He did not receive any adjuvant therapy and was alive and doing well at 2 months after adhesiolysis and during follow-up for 6 months after surgery with no evidence of recurrence or metastasis.

3. Discussion

Primary SCC arising in the urinary tract is an uncommon neoplasm, and the urinary bladder and male urethra are more frequent sites of SCC than the kidney [11]. Until recently, SCC of the urinary tract was

Table 1
Summary of published cases of primary squamous cell carcinoma of the kidney.

	Author	Sex	Age (years)	Presentation	Location	Treatment (+adjuvant therapy, if received)	Tumor extent	Renal stone	Involvement of renal pelvis	Prognosis
1	Terada (2010)	M	73	Hematuria and lumbago	Multiple: bladder, left ureter, and left kidney	Cystectomy and nephroureterectomy	NA, replacing entire kidney parenchyma	Absent	Absent	Alive and disease free at 3 months after surgery
2	Kulshreshtha (2012)	F	60	Weight loss for 3 months	Mid and lower pole of the left kidney	Radical nephrectomy with lymph node dissection	6.5 × 5.5 cm, with Gerota's fascia invasion and para-aortic lymph node metastasis (pT4N1)	Absent	Absent	Alive and disease free at 13 months after surgery
3	Ghosh (2014)	M	51	Dull and intermittent flank pain for 5 months	Lower pole of the right kidney	Radical nephrectomy	5.8 × 5.5 cm (pT1bN0)	Absent	Absent	Alive and disease free at 12 months after surgery
4	Sahoo (2015)	F	50	Right abdomen pain for 6 months	Upper pole of the right kidney	Radical nephrectomy	8.0 × 6.0 cm (pT2aNx)	Absent	Absent	Alive and disease free at 6 months after surgery
5	Wang (2016)	M	61	Hematuria and lumbago for 2 months	Right kidney	Radical nephrectomy	NA, with perirenal fat invasion (pT3aNx)	Absent	Absent	Alive and disease free at one month after surgery
6	Zhang (2020)	F	61	Intermittent flank pain for 2 months	Lower pole of the right kidney	Radical nephrectomy	NA, with perirenal fat invasion (pT3aNx)	Absent	Absent	Alive and disease free at 3 months after surgery
7	Fotovat (2021)	F	41	Flank pain and dysuria for 3 months	Lower pole of the left kidney	Radical nephrectomy (+adjuvant chemotherapy with cisplatin and gemcitabine)	NA, with perirenal fat invasion and para-aortic lymph node metastasis (pT3aN1)	Present	Absent	Metastasis to ovary at 8 months after surgery
8	Present	M	61	Flank pain and weight loss for 2 months	Lower pole of the right kidney	Radical nephrectomy with right hemicolectomy	9.0 × 8.0 cm, with ascending colon invasion (pT4N0)	Present	Absent	Alive and disease free at 5 months after surgery

Abbreviations: NA, not applicable.

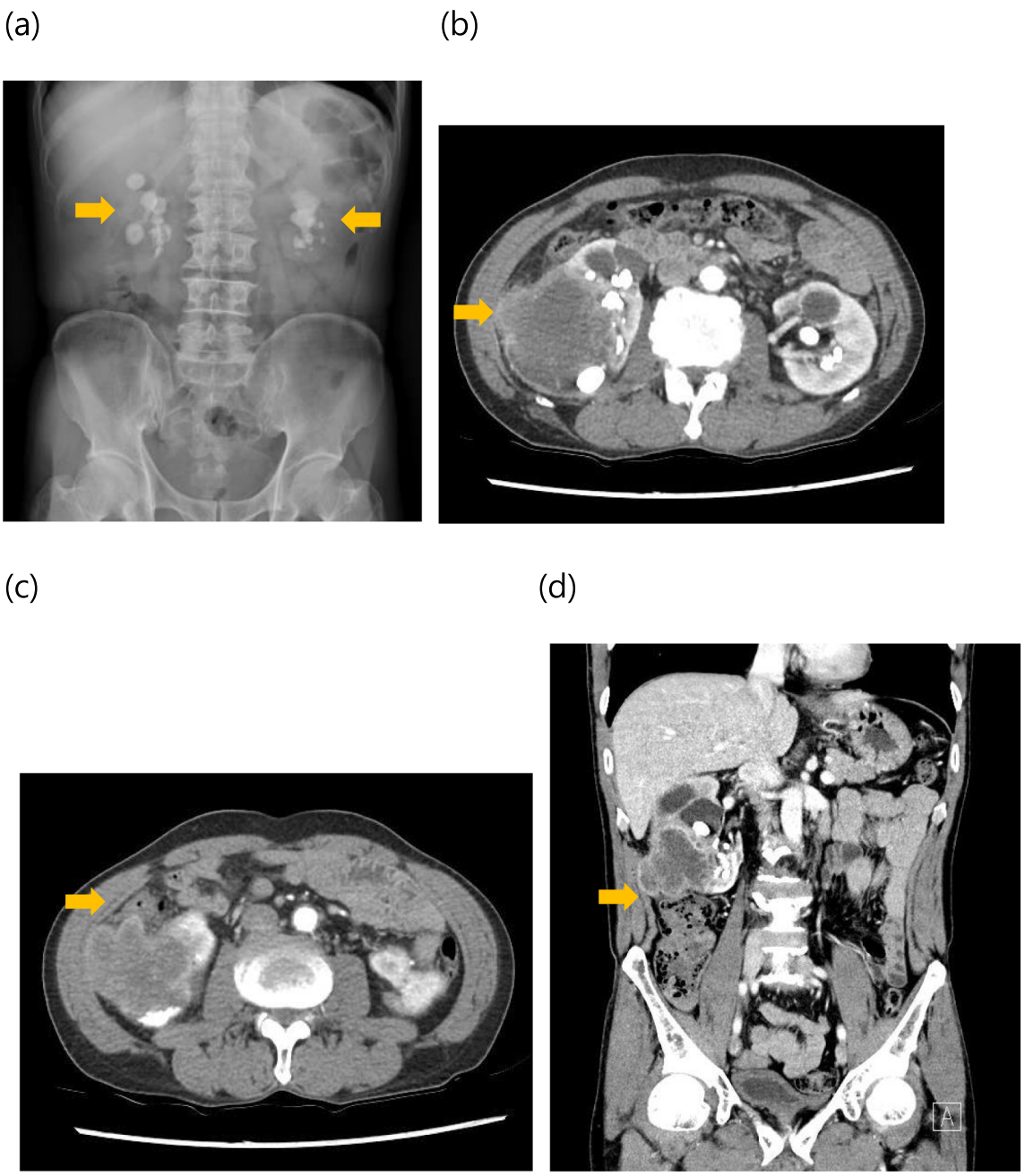

Fig. 1. (a) X-ray of the kidneys, ureters, and bladder showed multiple renal stones and staghorn stones in both kidneys. Contrast-enhanced computer tomography showed a large mass in the right kidney. The mass invading into the perirenal fat tissue (b) and ascending colon (c and d).

considered to arise from a process of metaplasia, particularly keratinizing squamous metaplasia of the urothelium [8,12]. In the presence of coexisting urothelial dysplastic lesions, including urothelial CIS, the tumor should be diagnosed as urothelial carcinoma with squamous differentiation. Therefore, the urothelium of the renal pelvis should be histologically normal for the diagnosis of primary SCC of the kidney parenchyma. Squamous metaplasia of the urothelium is considered to result from chronic irritation, including renal stones, infection, endogenous and exogenous chemicals, hormonal imbalance, and vitamin A deficiency [2]. However, the mechanism of SCC of the kidney parenchyma remains unclear.

To confirm the diagnosis of primary SCC of the kidney parenchyma, metastatic SCC from any other site should be ruled out by evaluating clinical history, imaging studies, and microscopic examination. Although the patient in the present case had multiple renal stones, which are known risk factors, there was no pathologic evidence of urothelial neoplasm or squamous metaplastic and/or dysplastic changes in the urothelium despite extensive sampling of the pelvicalyceal system. In addition, CT revealed a solitary mass in the kidney, and FDG-PET/CT failed to detect any other primary sites. Hence, a diagnosis of primary SCC of the kidney parenchyma was confirmed.

Histologically, renal SCC is similar to SCC of other sites, such as the lung or head and neck region, and it consists of sheets of atypical squamous cells, intercellular bridges, and keratin pearls.

Table 1 summarizes the results of a literature review of primary SCC of the kidney parenchyma. Eight cases, including our own, were identified. The prevalence was equal in men (4/8 cases) and women (4/8 cases), and the mean age was 52 years (range, 41–73 years). The major symptom was non-specific pain around the flank or lumbar areas. In contrast, urinary symptoms, including hematuria or dysuria, were

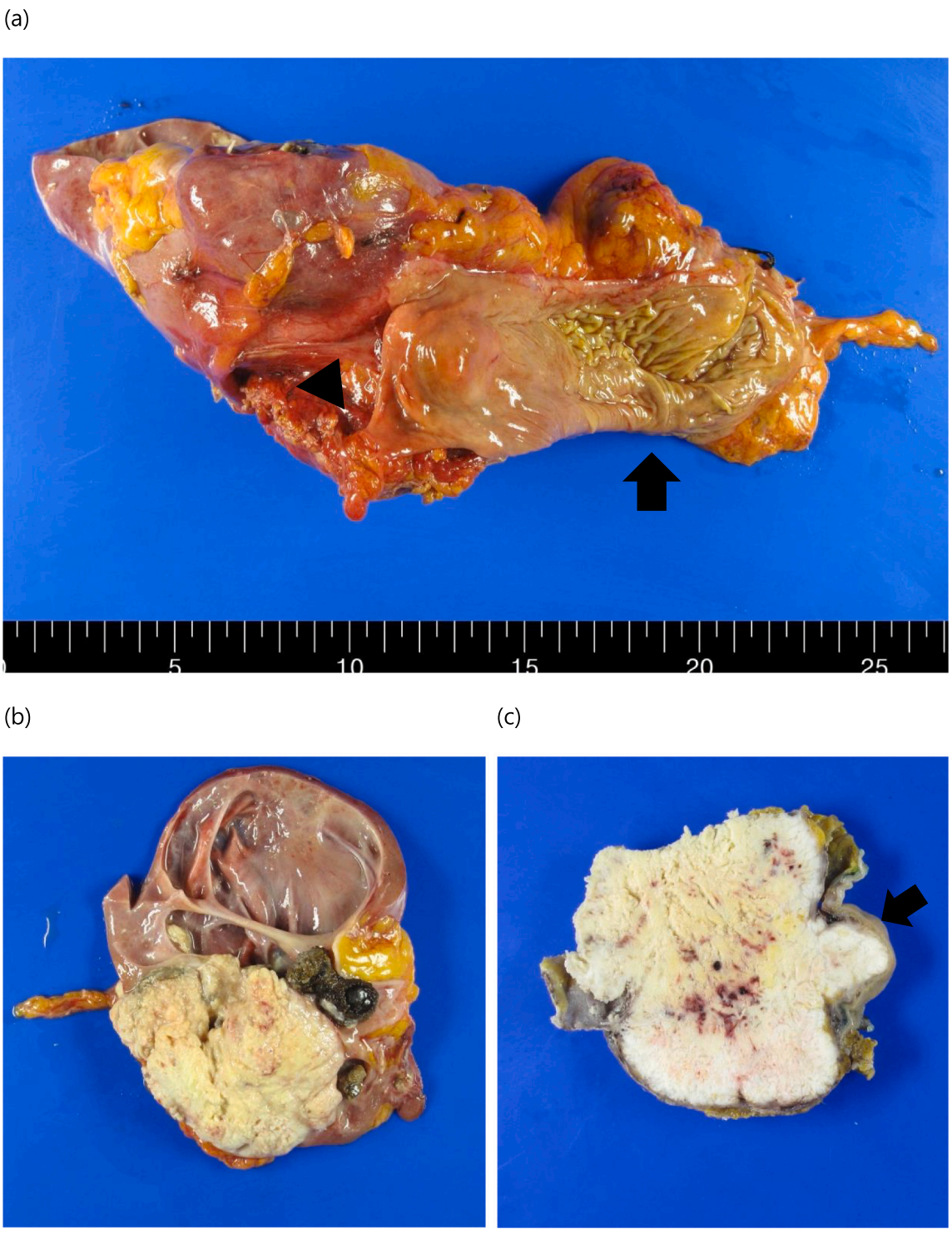

Fig. 2. On gross examination, (a) the ascending colon (arrow) was adhered to the right kidney (arrowhead). (b) The renal pelvis contained multiple renal stones resulting in hydronephrosis, and a well-defined yellow to white solid mass was identified in the lower pole. (c) On the cut surface, the mass invaded into the colon wall (arrow indicates colon mucosa).

observed in only three cases. Tumors were most commonly located on the right side (5/8 cases) and the lower pole of the kidney (5/8 cases). Although two cases were associated with renal stones, the renal pelvicalyceal system was histologically normal in all cases. More than half of the cases (5/8 cases) had an advanced tumor stage (higher than pT3), of which two had lymph node metastases. Moreover, one patient who received adjuvant chemotherapy (case 7) had metastasis to the ovaries 8 months later. These results suggest that SCC of the kidney has poor prognosis. Although the prognosis of SCC is not different between patients with urothelial carcinoma and SCC of the same stage, as shown in Table 1, patients with SCC tend to be diagnosed at a more advanced stage [13].

Because SCC of the kidney is extremely rare, there are no standard guidelines for management; radical nephrectomy tends to be the primary treatment, even in patients with metastatic disease [14]. The efficacy of adjuvant treatment was marginal, as observed in case 7 with

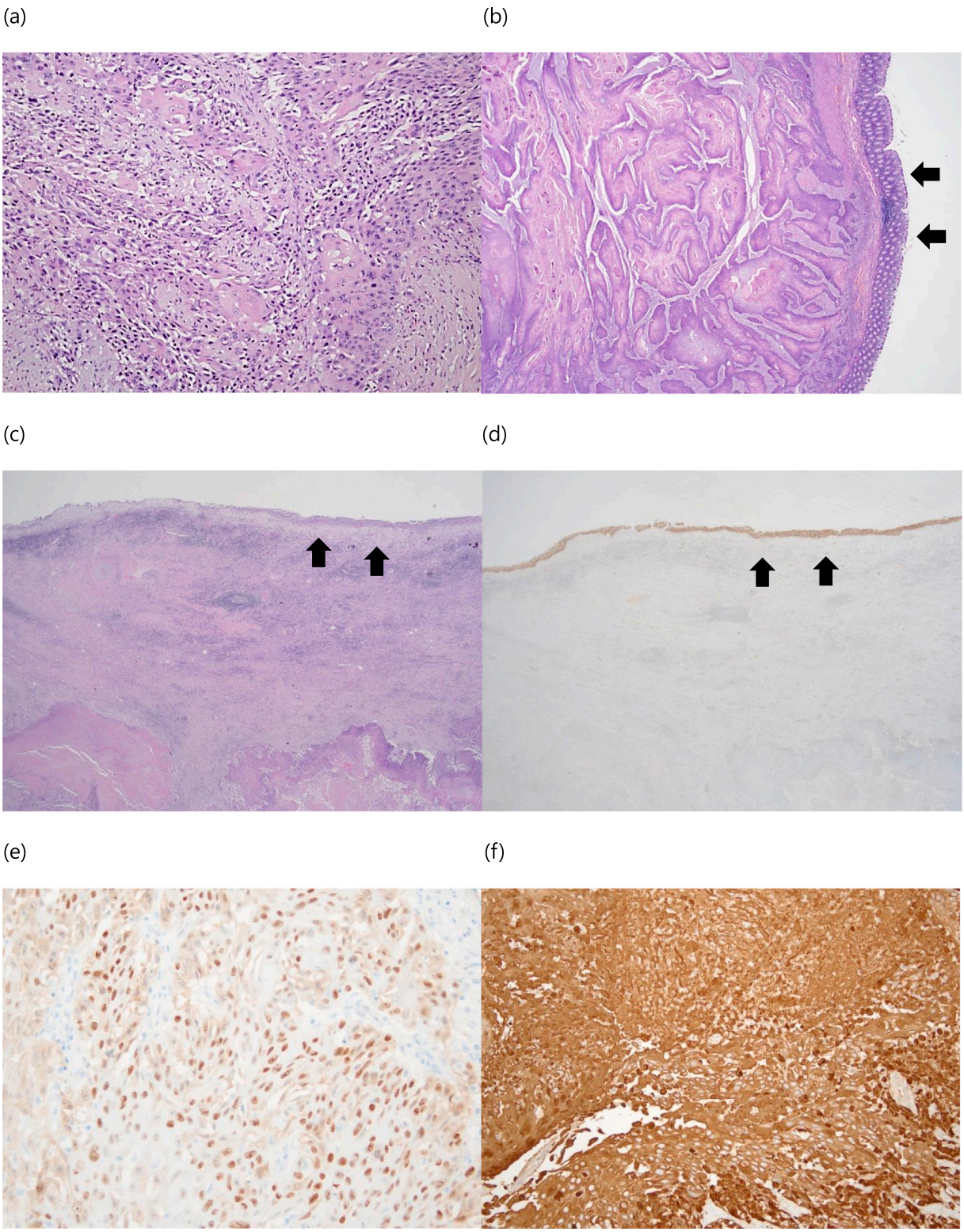

Fig. 3. (a) Proliferation of atypical squamous cells with keratin pearls and desmoplastic stroma. Histologically, the mass was consistent with well-differentiated squamous cell carcinoma (SCC) (×100). (b) SCC invading into the submucosal layer of the colon wall (arrow indicates colon mucosa, ×1.25). (c–d) (×1.25) The urothelium of the renal pelvis was histologically normal (arrow), and immunohistochemistry of the urothelium was positive for GATA3. Immunohistochemistry of the tumor was positive for p63 (e) and CK5/6 (f) (×100).

distant metastasis despite adjuvant chemotherapy [4]. Although the number of cases is small, it is interesting to note that the patients with metastasis are the youngest (case 7). The patient in the present case was old age and referred at advanced stage. Then, a surgical margin-negative R0 resection was performed. There were minor complications after surgery, but no local recurrence or metastasis. In accord with this observation, younger patients need to recognize the risk of metastasis and to follow-up more closely.

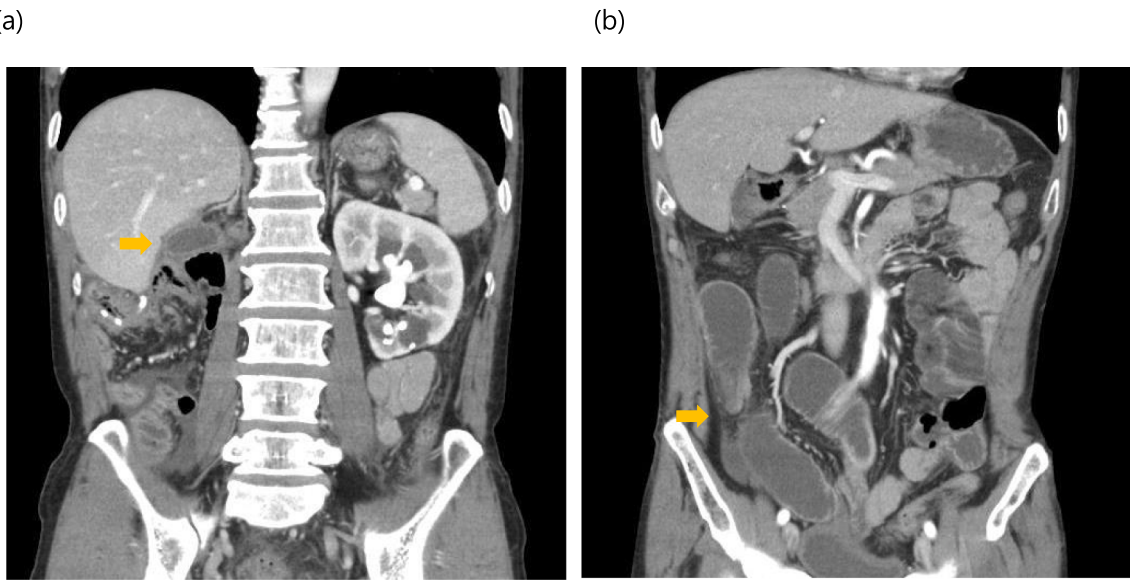

Fig. 4. Contrast-enhanced computer tomography showed peripheral enhancing fluid collection in pervious operation site (a) and abrupt narrowing and distension of small intestine (b).

Another treatment option for patients with receptor-positive primary SCC of the kidney is anti-EGFR therapy; however, additional studies are required to clarify the role of anti-EGFR therapy in this patient population [15].

4. Conclusion

Primary SCC of the kidney parenchyma is a rare neoplasm. We present an interesting case of ascending colon invasion in a 61-year-old man. Owing to its rarity, primary SCC of the renal parenchyma tends to be diagnosed at a more advanced stage than other primary kidney cancers. Traditionally, radical nephrectomy with or without lymph node dissection has been performed as the primary treatment, but the management of primary SCC of the kidney remains inconclusive owing to limited studies on its incidence, etiology, and clinical course. Additional long-term follow-up studies are needed to inform diagnostic and treatment decisions.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Ethical approval

This case report was approved by the institutional review board of our institution (IRB No. HPIRB 2021-07-031).

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Joo Yeon Kim: Conception and design of the study, drafting the article, and final approval.
Cheol Kyu Oh: Acquisition of data, manuscript revision.

Declaration of competing interest

The authors report no conflict of interests.

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