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Case Report

Procedure Triggers Rapid Progression of Renal Cell Carcinoma

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Abstract.

We present two renal cell carcinoma (RCC) cases with rapid disease progression within one month of an interventional procedure. Analysis of the clinical courses and laboratory data suggested that a burst of inflammatory cytokines following the procedures could have been the main reason for cancer progression. Higher tumor burden and the presence of paraneoplastic syndrome could be indicators predicting such a complication. Although the mechanism is not well understood, identifying such patients is important.

Keywords **:** renal cell carcinoma, procedure related complication

病例報告

因術式引發腎細胞癌快速惡化

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中文摘要

腎細胞癌本身疾病進展緩慢，但本次報告內容則提出因檢查而導致腫瘤快速進展的特殊個案。根據病患的血液檢查，推測可能與發炎性細胞激素誘導有關，而容易引起大量細胞激素釋放的相關因子有診斷時腫瘤大小與是否有腫瘤附屬症候群相關，但準確之原因仍需進一步探討。臨床上遇到此類患者在安排檢查時須特別注意。

關鍵字: 腎細胞癌、檢查引發之併發症

INTRODUCTION

Accelerated cancer progression after local treatment has been previously reported in different types of cancer. Seki T et al. presented a hepatocellular carcinoma case whose condition deteriorated rapidly after undergoing locoregional therapy [1]. Tomoki Yamano et al. presented a case of gastric cancer progressing rapidly within three months of endoscopic biopsy [2]. No similar reports have been reported in renal cell carcinoma (RCC), although studies have focused on the risk factors of rapid progression following nephrectomy [3]. It is crucial for every clinical practitioner to explain the potential complications to the patient before a procedure. As a reminder of potential

complications, we report two patients with RCC showing extremely rapid progression after a relatively simple procedure.

CASE REPORTS

Case 1

A 43-year-old male patient was transferred to our hospital for histopathological diagnosis of a huge right renal tumor on November 11, 2011. Hepatitis C and alcohol related liver cirrhosis had been diagnosed 5 years earlier. His liver reserve and performance status were satisfactory when the renal tumor was diagnosed. Computed tomography (CT) revealed local advanced disease without distant metastasis. His laboratory data disclosed paraneoplatic syndrome, including anemia (hemoglobin: 10.8 (g/dL)) and borderline elevated C-reactive protein (4.043 mg/L). CT-guided fine needle biopsy was arranged for histological diagnosis. Just after biopsy, he developed lethargy, tachypnea (respiratory rate: 25/min), pyrexia, and mild hemoptysis. A slight rise in the C-reactive protein level (13.16 mg/L) was noted. A chest radiography revealed diffuse lung nodules (Figures 1A and 1B). An empiric antibiotic was prescribed because an infection, such as from a septic emboli, was suspected. The result of the first kidney biopsy was negative for malignancy, so a second fine needle biopsy was done on November 23, 2011. The final pathology showed RCC, clear cell type (Figures 1C and 1D). In the early morning of November 24, his condition deteriorated and he required full mechanical ventilator support in the intensive care unit. A follow-up CT revealed disseminated lung and brain metastases (Figure 2). Bronchoscopic biopsy was suggested, but the patient's family declined due to the risk of this procedure. The patient died of multiple organ failure on the 25th day after admission.

Case 2

A 45-year-old male patient had a left RCC diagnosed in January 2010. His initial tumor staging was stage IV with lumbar spine metastasis. Before he received anti-cancer therapy, he was admitted for epigastric pain. Physical examination disclosed no remarkable findings. The laboratory data revealed paraneoplatic syndrome, including leukocytosis (white cell count: 30.1 (10^3/uL)), anemia (hemoglobin: 11.9 (g/dL)), and elevated C reactive protein level (272.73 mg/L). Panendoscopy showed multiple gastric ulcers. Eight hours after the procedure, spiking fever, chillness, and conscious disturbance developed. Because of respiratory failure, he was intubated and transferred to the intensive care unit. Chest radiography post intubation showed multiple pulmonary nodules and a left pleural lesion (Figures 1E and 1F). The follow-up CT also confirmed rapid cancer progression (Figure 3). Pluera biopsy and pericardial effusion examination revealed atypical cells. However, because the samples were too small, further special staining could not performed. His condition deteriorated and he died of multiple organ failure on the 15th day after admission.

DISCUSSION

These two cases suggest the possibility of procedure-induced rapid RCC progression. Although final pathological confirmation of the metastatic sites could not be obtained, there were several reasons indicating that the deterioration of the patients' condition was associated with tumor progression. First, serial imaging studies showed rapid progression and even newly developed lesions (Figures 1-3). Both patients died due to target organ involvement, such as the heart, lung and brain. Second, the evidence of infection was

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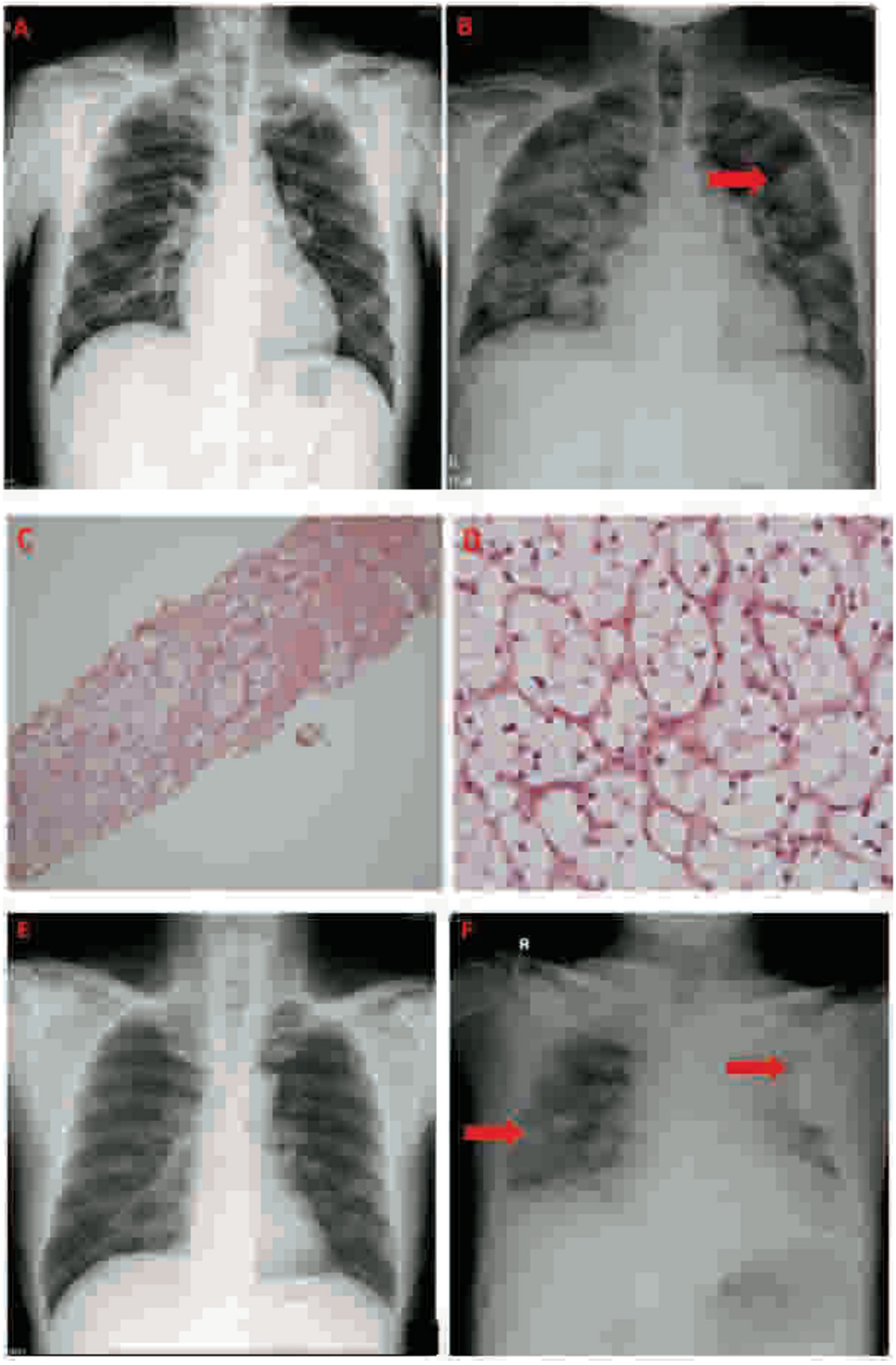

Figure 1. Pre-procedure (A) and post-procedure (B) chest radiography of case 1. Pathology in case 1 was renal cell carcinoma, clear cell type (C and D). Pre-procedure (E) and post-procedure (F) chest radiography of case 2

Table 1. Clinical course and laboratory data

	Diagnosis	Before procedure	After procedure	Procedure	Date of death
Case 1	Renal cell carcinoma	Hb: 10.8 g/dL CRP: 4.043 mg/L	Hb: 8.2 g/dL CRP: 13.6 mg/L D-dimer: 5300 FEU ng/mL	Fine needle biopsy, the 3rd day of admission	The 25th day
Case 2	Renal cell carcinoma	WBC: 30000/uL Hb: 8.7 g/dL CRP: 272.73 mg/L	WBC: 47200/uL Hb: 9.1 g/dL CRP: 297 mg/L D-dimer: >10000 FEU ng/mL	Panendoscopy, the 1st day of admission	The 15th day

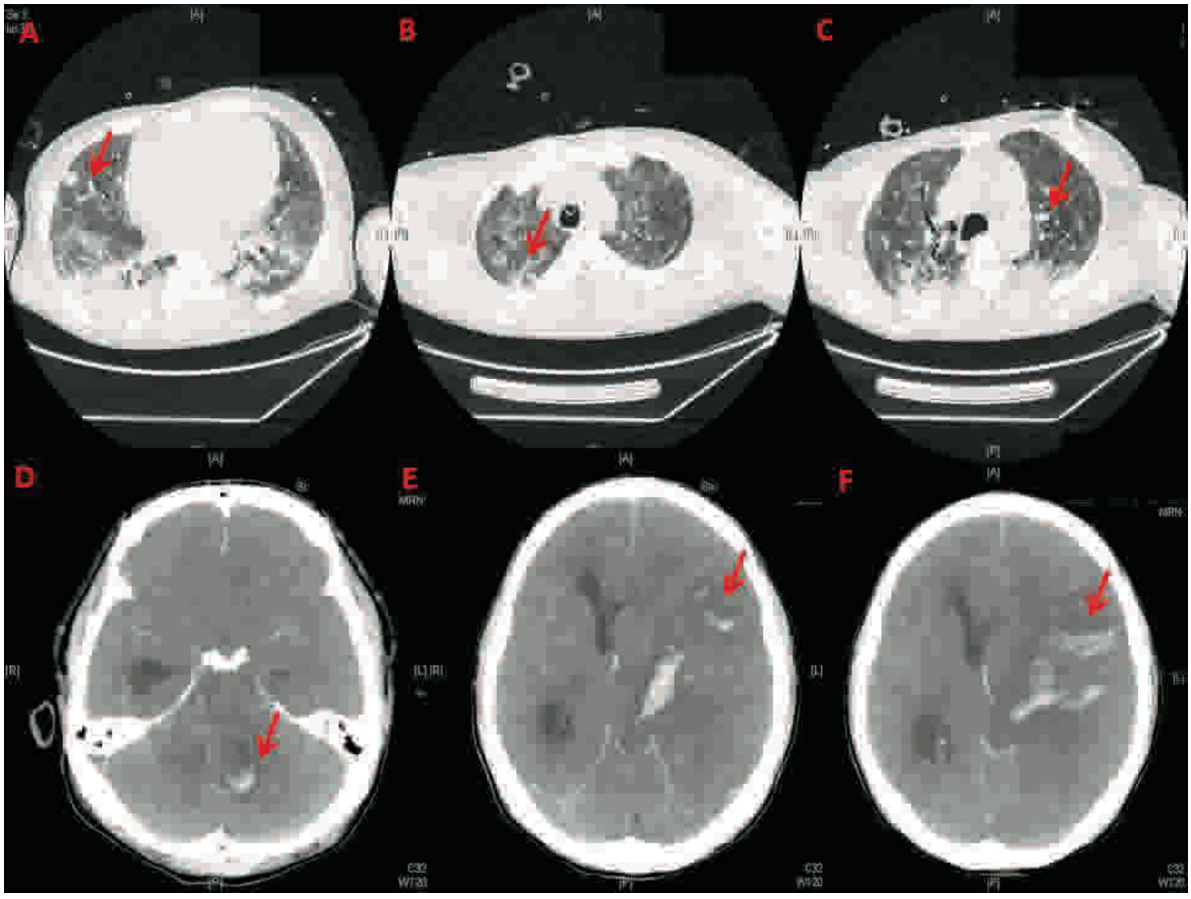

Figure 2. Computed tomography images for case 1: bilateral lung metastases (A-C) and multiple brain nodules (D-F)

insufficient, not only because the culture results were negative, but also because the infection foci could not be determined. Third, the initial and final laboratory data showed paraneoplastic syndrome rather than active infection. Komai et al. reported that preoperative serum C-reactive protein could predict the prognosis of localized RCC [4]. Thus, based on the serum C-reactive protein levels, a correlation between the procedures and serum cytokine level could be found (Table 1). Patients with RCC frequently have parane-

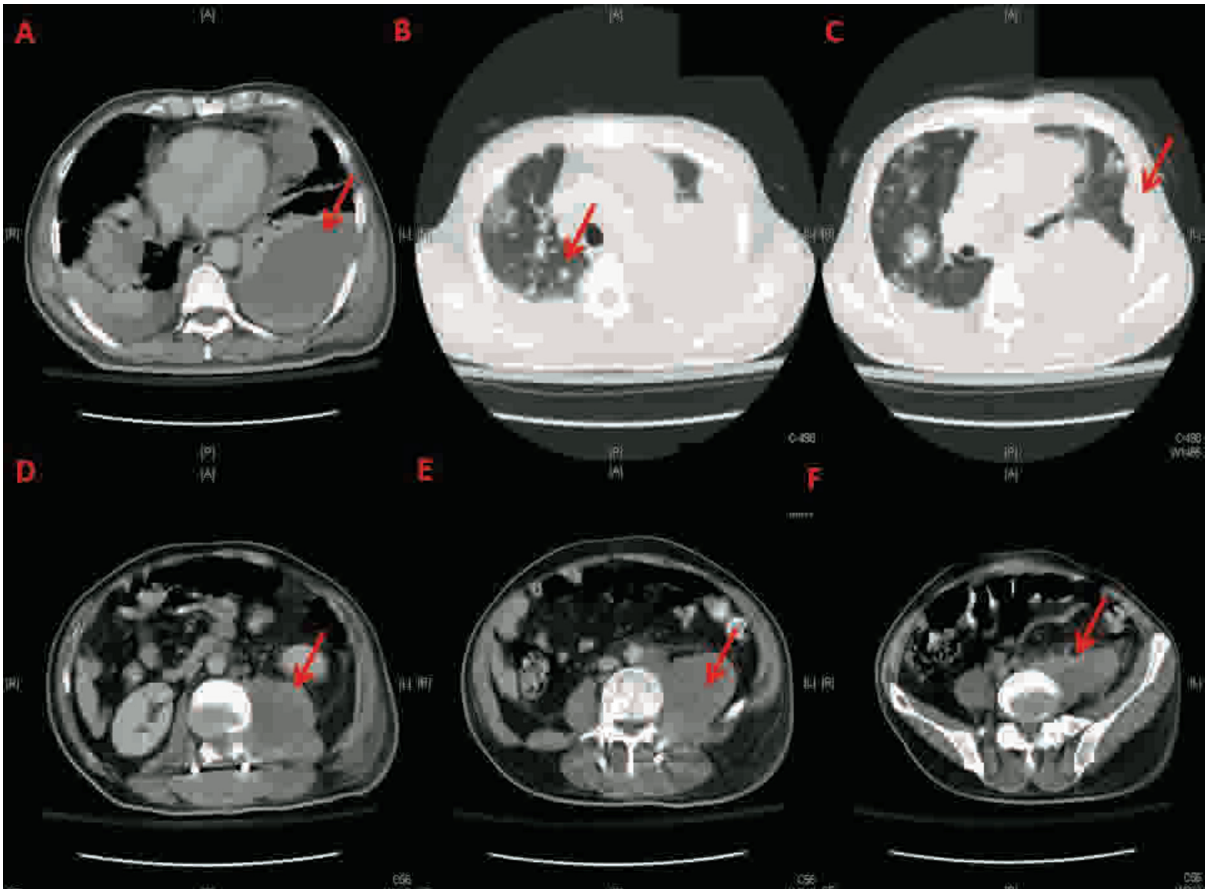

Figure 3. Computed tomography images for case 2 showing metastases to lung, left pleura, lumbar spine, abdominal nodes and left psoas muscle (A: left pleural mass, B: multiple lung nodules, C: left pleural mass, D: left infiltrating psoas mass and multiple abdominal nodes, E: left infiltrating psoas mass with bony structure involvement, F: left infiltrating psoas mass extending to sacral area)

oplatic syndrome, which may due to the higher level of circulating interleukin-6 or other cytokines [5]. This supported our hypothesis that tumor progression affected survival in both patients.

It is crucial to figure out which types of RCC would have such kind of progression pattern and how this risk is induced. There were similar characteristics in both patients, including male gender, large tumor burden or advanced stage, and the presence of paraneoplastic syndrome. However, there was no direct evidence linking the procedures with RCC progression. Dysregulation of signaling pathways could explain tumor progression in these cases. RCC has been reported to be related to the hypoxia-inducible pathway [6]. Stimuli from a procedure could induce transient hypoxia, which in turn could trigger hypoxia responsive gene transcription. Stimulation of hypoxia indicible trascription factors, such as vascular endothelial growth factor, may lead to rapid tumor progression [7,8]. Alternatively, the NF-κB pathway is also known to be involved in the pathogenesis of RCC, and it could be activated and amplified by a hypoxia event [9]. NF-κB plays a critical role in explaining tumor progression because of its association with cytokines, such as interleukin-6, which are related to paraneoplastic syndrome [5,10]. Both cases displayed

paraneoplastic syndrome at first diagnosis. A rise in cytokine secretion may occur after a procedure, which could also explain tumor progression. However, RCC is a biologically complex disease. Papillary RCC, for example, is associated with the mesenchymal epithelial transition pathway rather than the hypoxia inducible pathway [11]. Thus, it is important to determine which kind of event is associated with which pathway.

Elucidating the mechanisms of tumor progression could help the identification of possible preventive strategies. The use of anti-vascular epithelial growth factor agent as a prophylactic agent is not considered because of its cost and uncertain efficacy. However, corticosteroids have been used as a treatment modality under the hypothesis of NF-κB, so could serve as a prophylactic agent [10,12]. However, the efficacy of prophylactic treatment is not yet known, and further studies in this field are necessary.

In conclusion, we report two cases of procedure-induced RCC progression. Even though the mechanism is not fully understood, physicians should be aware of this possibility in their management of RCC patients.

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