Clinical Case Report

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Serial renography for evaluation of the impact of capecitabine therapy on renal function

A case report

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Abstract

Rationale: Cancer can cause renal dysfunction and disease either directly or indirectly, through adverse effects of therapies, including chemotherapy and radiation. The assessment of renal function in cancer patients is necessary in clinical practice.

Patient concerns: A 31-year-old woman had proctoscopy performed in our hospital for a principal complaint of bloody stool for 6 months and worsening 1 month prior to presentation.

Diagnoses: Following proctoscopy, she was diagnosed with a signet-ring cell carcinoma of the rectum. Hartman surgery was performed. Metastasis of the carcinoma to regional lymph nodes around the rectum was verified by postoperative pathology.

Interventions: The patient was treated with capecitabine, and renal function was monitored over the course of treatment by renography before, during, and after chemotherapy.

Outcomes: We found that capecitabine caused a reversible decline of renal function. However, the value of blood urea nitrogen (BUN) and serum creatinine (Cr) remained within the normal range during chemotherapy. The patient's chemotherapy regimen was altered after her oncologists concluded that she was developing nephrotoxicity from capecitabine. She was treated with tegafur, gimeracil and oteracil potassium capsules. This patient was followed over the next 6 months, and no abnormal renal function re-occurred.

Lessons: Our experience with capecitabine shows that dosing adjustments can be warranted for chemotherapy in cancer patients, requiring monitoring of renal function. Renography may provide an early warning to protect the renal function of tumor patients when they receive chemotherapy.

Abbreviations: 5-Fu = 5-fluorouracil, BSA = body surface area, BUN = blood urea nitrogen, Cr = serum creatinine, CT = computed tomography, DT5000, cGy/25F = dose total 5000, centigray/25 Frequency, GFR = glomerular filtration rate, MBq = megabecquerels, SPECT = single-photon emission computed tomography, Tc-99m DTPA = 99m-technetium diethylenetriaminepentaacetic acid.

Keywords: capecitabine, chemotherapy, renal function, Tc-99m DTPA renography

1. Introduction

It is well known that use of cytotoxic drugs for cancer chemotherapy can lead to nephrotoxicity and decline of renal function. However, chemotherapy for patients with malignant tumors is necessary and can be life-saving in the clinical setting. Clinicians need to strictly control the dose of chemotherapy agents and regularly check hepatic and renal function for cancer patients undergoing chemotherapy with many of the widely used anti-neoplastic agents.

2. Case presentation

A 31-year-old woman had proctoscopy performed in our hospital for a principal complaint of bloody stool for 6 months and worsening 1 month prior to presentation. Following proctoscopy, she was diagnosed with a signet-ring cell carcinoma of the rectum. Hartman surgery was performed. Metastasis of the carcinoma to regional lymph nodes around the rectum was verified by postoperative pathology. She was subsequently treated with chemotherapy and pelvic radiotherapy (DT5000 cGy/25F)

2.1. Clinical findings

Laboratory tests (Table 1) obtained with each renography showed normal levels of blood urea nitrogen (BUN normal range = 2.9 to 8.2 mmol/L), and creatinine (Cr normal range = 45 to 84 mmol/L). The patient had no history of diabetes or hypertension, and no known renal disease. An abdominal computed tomography (CT) indicated that both kidneys were normal in shape and size.

Tc-99m DTPA renography was performed on July 23 (Fig. 1A and B), July 28 (Fig. 1C and D), and August 18 (Fig. 1E and F), respectively. The patient ingested 500 ml of water 30 minutes before renography and sat on the chair in front of a single-headed

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Table 1

There were GFR values and lab values in 3 renography sessions of this patient.

Renography	Date	GFR (left kidney)	GFR (right kidney)	Cr	BUN
1	July 23th	67.56	53.62	41	3.5
2	July 28th	34.13	40.19	47	4.2
3	August 18th	63.48	49.26	45	4.9

Tc-99m DTPA renography was performed on July 23, July 28, and August 18, respectively. Laboratory tests obtained with each renography showed normal levels of blood urea nitrogen (BUN normal range = 2.9–8.2 mmol/L), and creatinine (Cr normal range = 45–84 mmol/L). The GFR values of the first renography for the left and right kidney were 67.56 and 53.62, respectively. The Cr value was 41 and the BUN value was 3.5. The GFR values of the second renography for the left and right kidney were 34.13 and 40.19, respectively. The Cr value was 47 and the BUN value was 4.2. The GFR values of the third renography for the left and right kidneys were 63.48 and 49.26, respectively. The Cr value was 45 and the BUN value was 4.9.
GFR = glomerular filtration rate, BUN = blood urea nitrogen, Cr = serum creatinine.

gamma camera (GE Infinia IISPECT/CT). The camera detector was located behind the chair, 5 cm from the patient. The radiochemical purity of the Tc-99m DTPA was greater than 98%, and for the 925 MBq was injected into an antecubital vein. A nuclear medicine specialist evaluated the images and data. Glomerular filtration rate (GFR) values were normalized by BSA (body surface area) using Gates' method, which was programmed into the SPECT computer, and calculations were performed automatically from the renal dynamic images using the following formula: GFR $(\text{mL/min}/1.73\,\text{m}^2) = (9.817270 \times \text{renal uptake percentage} - 6.82519) \times 1.73/\text{BSA}$.[1]

In the first renography, the glomerular filtration function and renal excretion function were within normal limits. The patient was then treated with chemotherapy for 14 days

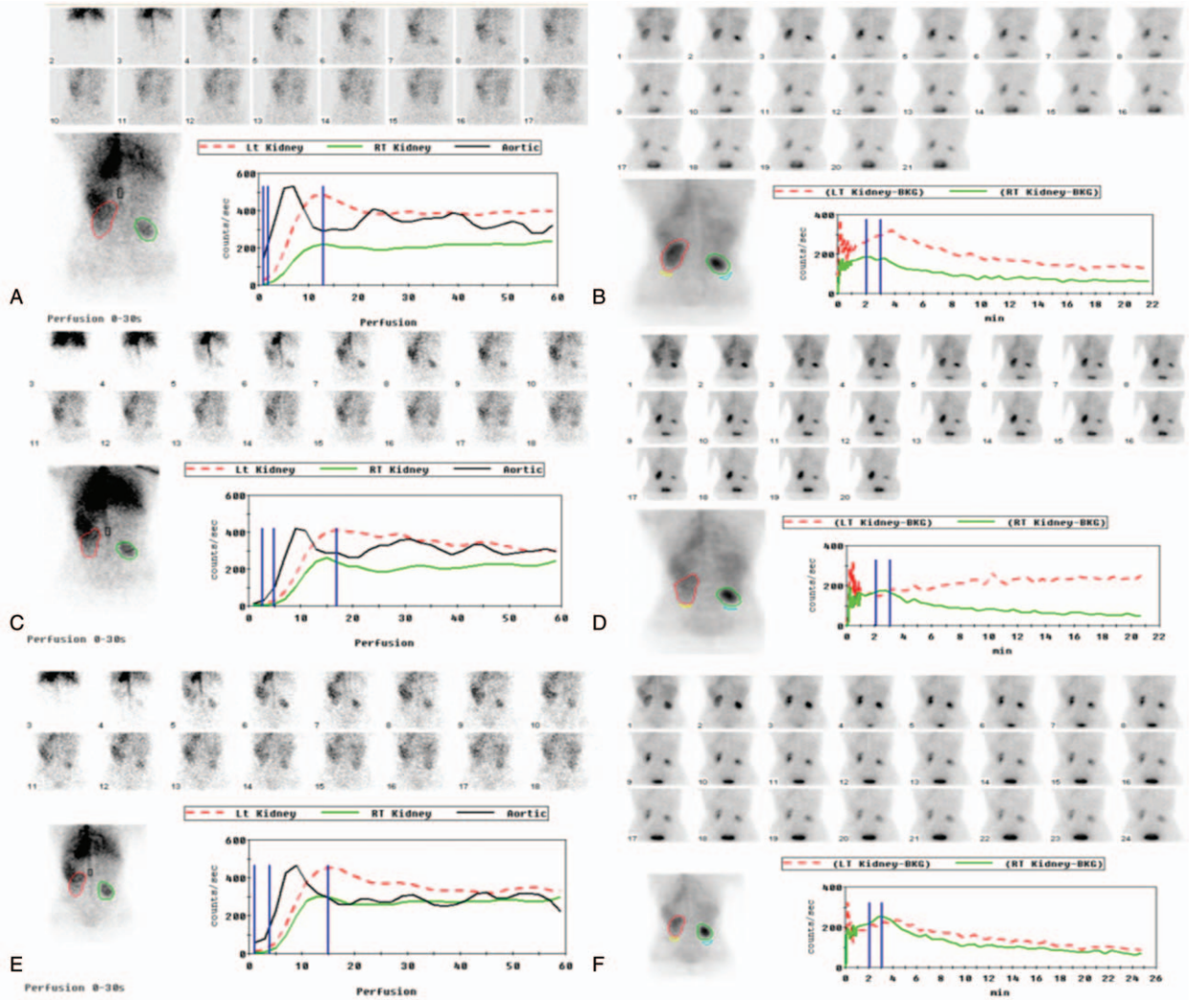

Figure 1. There were 3 renographies of this patient. (A, B) The results of the first renography. The renal excretion curves were (regard as) normal. (C, D) The results of the second renography. The excretion curve for the left kidney became high following treatment with capecitabine for 4 days. (E, F) The results of the third renography. This renography revealed that the renal function had almost returned to normal, especially for the left kidney (The *Y*-axis depicts mean radioactive counts per second, and the *X*-axis shows time.).

after the first renography. The second renography, performed 4 days later, during chemotherapy, revealed a decline of GFR, especially in the left kidney. These changes may be attributed to the effects of capecitabine. The renal function (GFR of both kidneys) then returned toward her baseline levels when the third renography was performed on August 18, 11 days after she had completed the course of capecitabine.

2.2. Follow-up and outcomes

The patient's chemotherapy regimen was altered after her oncologists concluded that she was developing nephrotoxicity from capecitabine. This patient was treated with tegafur, gimeracil and oteracil potassium capsules (80 mg/m^2/day, bid, d1–14), each cycle was repeated every 21 days. However, the laboratory chemistry results revealed that the changes in Cr and BUN did not change significantly and remained within the normal range before and after chemotherapy. The patient needed reconstruction of her fistula because a neoplastic mass was found around the original fistula after 5 cycles of chemotherapy and conservative treatment. She was followed over the next 6 months, and no abnormal renal function re-occurred.

Ethical approval was given by the medical ethics committee of Shandong Cancer Hospital affiliated to Shandong University. The patient has consented for the publication of the present case report.

3. Discussion

Cancer can cause renal dysfunction and disease either directly or indirectly, through adverse effects of therapies, including chemotherapy and radiation.[2] Over half of patients with cancer have renal insufficiency and as a result may require dose adjustment of anticancer treatments,[3] making serial assessment of renal function necessary for oncology patients in clinical practice.

The most frequently applied index of renal function is serum Cr, although GFR is accepted as the best overall measure of renal function.[4] Additionally, Tc-99m DTPA renography has been introduced into clinical practice, with proven ease of operation and good repeatability, although it provides a less accurate determination of GFR than the inulin continuous perfusion method.[1,5] It is generally accepted that renal radioactive tracers are not at all nephrotoxic. In the current case, renal function was determined by Tc-99m DTPA clearance, the standard technique for use in adult patients presenting for chemotherapy.[6]

Capecitabine is an orally inactive pro-drug for 5-fluorouracil (5-Fu). There are some peculiarities in resulting distributions of 5-Fu in the organism that result from variations in the distribution of thymidine phosphorylase. This enzyme metabolizes capecitabine, converting it into 5-Fu and other metabolites, and is overexpressed in tumor cells. Capecitabine and its metabolites are predominantly eliminated by the kidney,[7,8] and about 95% of the administered dose appears in the urine.

Currently, capecitabine is widely used in the adjuvant and palliative treatment of different tumors. It is administered orally twice daily, and the present patient was treated with 2-gram doses. In her case, the second renography showed that the GFR had declined (especially in the left kidney), indicated that capecitabine effects on renal function and reduction of the secretory function of the renal tubules. The third Tc-99m DTPA renography revealed that after completion of therapy renal function recovered significantly toward the original level, including the GFR and the excretion curve. This documents that the effects of capecitabine on renal function are transient and reversible.

The results also suggest that renography was a more sensitive indicator of the nephrotoxicity of capecitabine than were the standard laboratory blood tests (Cr and BUN) for renal function. The serum levels of these metabolites reflect their total body burden, whereas the GFR estimated by renography directly represents the function of each of the kidneys. It seems clear from the renography results that both the left and right kidneys were damaged to some extent after chemotherapy, but that the Cr and BUN remained in the normal range as a result of renal compensatory mechanisms. Thus, serial use of the routine blood tests for kidney function provided no evidence that renal toxicity had in fact developed and then resolved in our patient. This finding justified the use of bilateral renography in this setting.

Capecitabine is regarded as safe for use in patients with normal renal function, but for those with evidence of renal failure, the dose is often reduced. If renal function is sufficiently compromised, capecitabine may be contraindicated.[8] The present case also entailed concerns as to capecitabine-induced renal damage, and a strategy of dosage adjustment was considered to avoid renal insufficiency. The renal function of this patient was protected by promptly substituting different chemotherapy agents, because abnormal renal function was documented when she underwent renography. Our results indicate that for some patients renography is a more reliable technique for evaluation of kidney damage than standard blood tests such as Cr and BUN. It may provide an early warning to protect the renal function of tumor patients when they receive chemotherapy.

4. Conclusions

Our experience with capecitabine shows that dosing adjustments can be warranted for chemotherapy in cancer patients, requiring monitoring of renal function. Further studies are needed in order to fully understand whether Tc-99m DTPA renography can be widely applied to monitor the nephrotoxicity of cancer chemotherapy agents.

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