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Induction Chemotherapy for Cancer of Mandibular Gingival in a Patient with Solitary Kidney

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Abstract

Solitary kidney is congenital or acquired, and the main cause of the latter includes nephrectomy. Regardless of the causes, individuals with a solitary kidney may have renal dysfunction. However, limited data on antineoplastic effects on renal function are available in chemotherapy for head and neck cancer. In this report, we describe a case of a solitary kidney patient with mandibular gingival cancer who was treated with induction chemotherapy and surgery. A 55-year-old Japanese woman was referred to us with a persistent pain in the left mandible that lasted for a few months. Her medical history included right nephrectomy after a traffic accident in childhood. An incisional biopsy revealed well-differentiated squamous cell carcinoma. The patient was diagnosed with stage G3a chronic kidney disease. She underwent two cycles of induction chemotherapy with docetaxel, cisplatin, and 5-fluorouracil. The cisplatin dose was reduced by 25%, but the docetaxel and 5-fluorouracil doses were not reduced. In both cycles, eGFR decreased, and serum creatinine transiently increased on Day 12; however, her renal function was restored at the end of each cycle. Then she underwent left mandibulectomy, buccal mucosa and partial maxillectomy, reconstructive surgery with a submental island flap. No infiltrative squamous cell carcinoma, sign of recurrence and aggravation of kidney function were observed. This suggested that, in patients with a solitary kidney, reduced cisplatin dose can show the favorable antineoplastic effect, maintaining renal function in the short term.

Keywords: Oral cancer; Solitary kidney; Induction chemotherapy; Cisplatin

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Introduction

Solitary kidney is congenital or acquired, and the main cause of the latter includes nephrectomy. Regardless of the causes, individuals with a solitary kidney may have renal dysfunction. However, limited data on antineoplastic effects on renal function are available in chemotherapy for head and neck cancer. Cisplatin is the standard of care for head and neck cancer and is frequently used for neoadjuvant and adjuvant chemotherapy. However, the main dose-limiting side effect is nephrotoxicity; therefore, the drug should be reduced in dosage or discontinued to prevent a reduction in urinary excretion and deterioration of renal function. In a solitary kidney, its function theoretically decreases to half, but compensatory renal hypertrophy can restore the function by about 70% of 2 kidneys. Nevertheless, the function may rapidly

deteriorate due to decreased renal blood flow or glomerular filtration rate. Here, we describe a case of a solitary kidney patient with mandibular gingival cancer who was successfully treated with induction chemotherapy with reduced cisplatin and surgery, maintaining the renal function.

Case Report

A 55-year-old Japanese woman was referred to our hospital with a persistent pain in the left mandible that lasted for a few months. Her medical history included right nephrectomy after a traffic accident in childhood. At the initial visit, an ulcer with induration extended from the lower left gingiva to buccal mucosa

was found (**Figure 1**). Computed tomography images showed a 25 mm × 20 mm × 10 mm expansive mass in the anterior border of the mandibular ramus and no lymphadenopathy in the head and neck region (**Figure 2**). An incisional biopsy revealed well-differentiated squamous cell carcinoma (**Figure 3**). The tumor was classified as cT2N0M0, stage 2, by using TNM classification for head and neck cancer. Based on these findings, we planned to perform induction chemotherapy and surgery. Blood chemistry tests revealed a creatinine level of 0.78 mg/dL, an estimated glomerular filtration rate (eGFR) of 59.6 mL/min/1.73 m² and a 24-hour creatinine clearance of 59.4 mL/min. As a result, she was diagnosed with stage G3a chronic kidney disease. She underwent two cycles of induction chemotherapy with docetaxel, cisplatin, and 5-fluorouracil (TPF). Because of her renal function, the dosage of cisplatin was reduced by 25% (75 mg/m² × 75%), but no alteration in that of the docetaxel (75 mg/m²) and 5-fluorouracil (750 mg × 5 days). In both cycles, neutrophil nadir counts decreased <500 /mm³ (Grade 3) on Day 9, eGFR decreased (50.9 to 43.0 mL/min/1.73 m²), serum creatinine transiently increased (0.9 to 1.05 mg/dL) on Day 12; however, her renal function was restored at the end of each cycle (**Figure 4**). Also, she often had nausea and vomiting, but no treatment was provided for these side effects. After the chemotherapy, she underwent a left mandibulectomy, buccal mucosa and partial maxillectomy, reconstructive surgery with a submental island flap. No deterioration of the renal function was observed during and post-surgery. No infiltrative squamous cell carcinoma was histopathologically found in the resected tumor, or deterioration was observed in her renal function (**Figure 5**).

Discussion

The main causes of acquired solitary kidney after a unilateral nephrectomy include living kidney donation, kidney cancer, and trauma. A reduced renal mass may increase intraglomerular pressure and glomerular hyperfiltration, causing glomerular damage with hypertension, albuminuria and glomerular dysfunction that result in the end of stage kidney disease. In renal

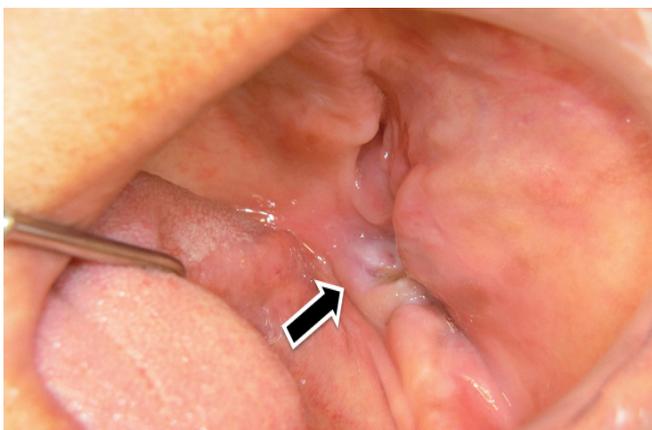


Figure 1 Intra-oral finding at the first visit. An ulcer with induration extended from the gingiva of the left mandible to the buccal mucosa (arrow).

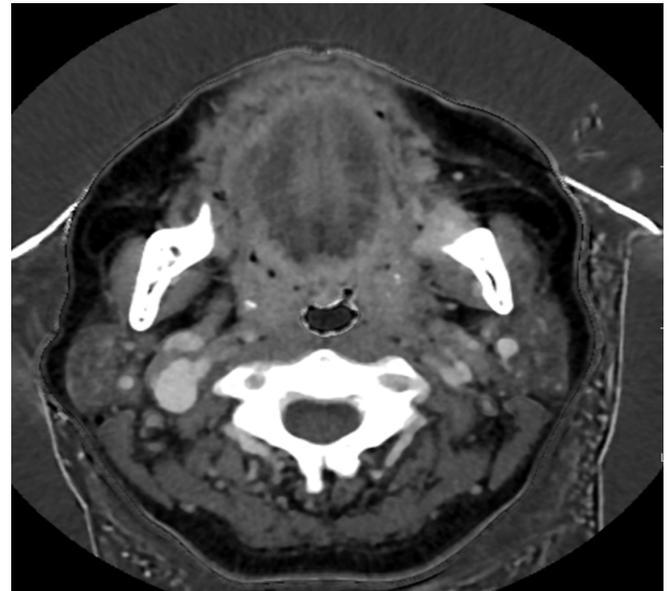


Figure 2 Computed Tomography (CT) findings. The dual-energy CT with iodine density image showing an expansive mass in the anterior border of the mandibular ramus (arrow).

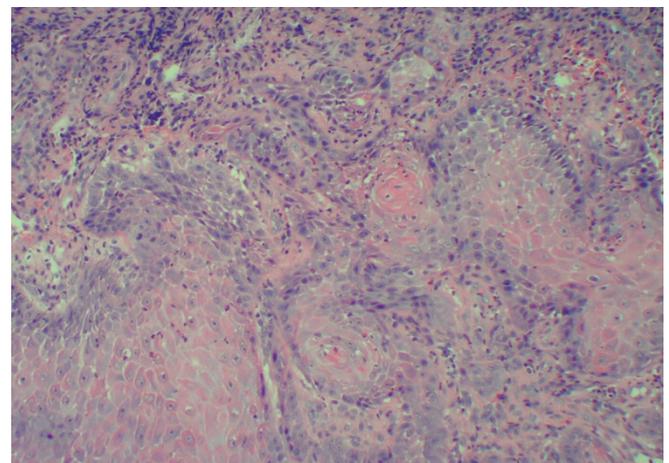


Figure 3 Histopathological findings in the biopsy specimen. The tumor cells formed a medium cancer cell nest and invaded into lamina propria (H&E, original magnification 400x).

trauma patients with unilateral nephrectomy, the incidence of acute renal failure is 5% to 10% [1], and the prevalence of chronic renal failure (CKD) or CKD progression is unknown. However, such patients are at higher risk for developing CKD, indicating that they are more likely to have acute kidney injury or aggravate underlying CKD [2]. In individuals born with or acquiring a solitary kidney in childhood, the contralateral kidney undergoes compensatory growth as a response to the loss of one kidney [3]. Such growth increased the remaining kidney volume by 188% of a healthy kidney within at least 4 years of life. The physiological growth of the remaining kidney is also achieved as documented in

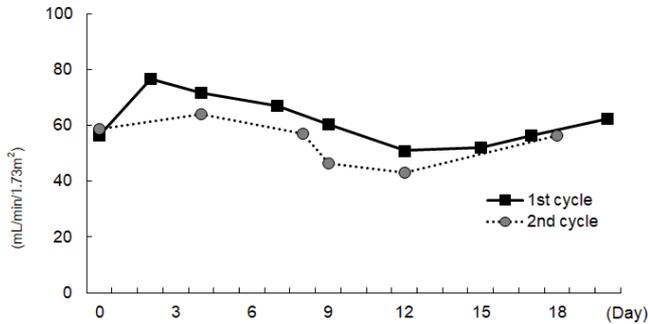


Figure 4a Change of estimated glomerular filtration rate during 2 cycles of chemotherapy.

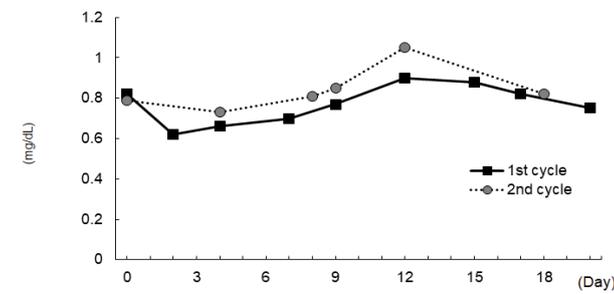


Figure 4b Change of creatinine during 2 cycles of chemotherapy.

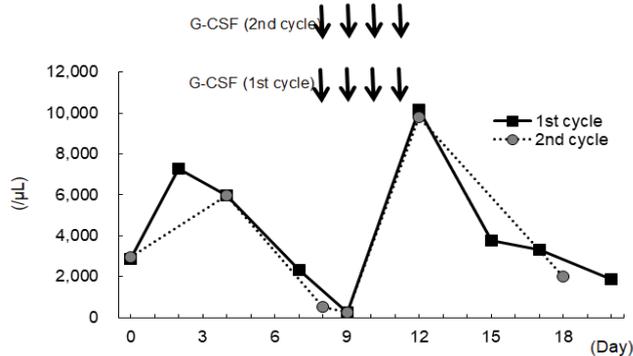


Figure 4c Change of neutrophil counts during 2 cycles of chemotherapy.

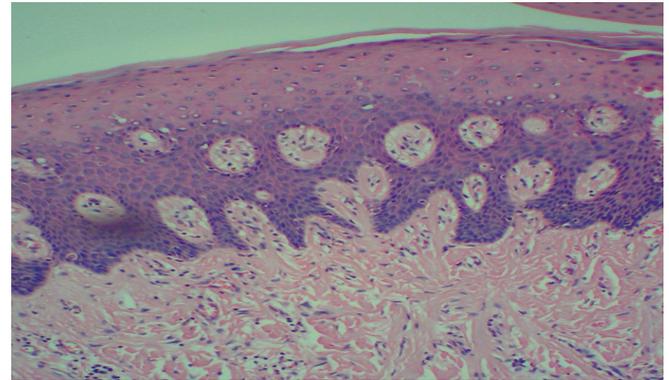


Figure 5 Histopathological findings of the resected specimen. No viable cancer cells were found in the resected tissues (H&E, original magnification 400x).a

Due to the nephrotoxicity of cisplatin, long-term cisplatin-based chemotherapy was reported to reduce renal function in patients with a solitary kidney after nephroureterectomy for the upper urinary tract urothelial carcinoma [6]. In this study, the dose of cisplatin was reduced by 25% when creatinine clearance (CrCl) was ≥ 50 mL/min and < 70 mL/min and by 50% when CrCl was ≥ 30 mL/min and < 50 mL/min. With this dosage regimen, long-term cisplatin-based chemotherapy can be used for patients with a solitary kidney without a serious adverse event (AE) and showed favorable antineoplastic effects. In the present study, the patient's baseline eGFR and CrCl were 56.4 mL/min and 59.4 mL/min/1.73 m², respectively. Therefore, only the cisplatin dose was reduced by 25%. In the two cycles, the patient's renal function decreased on Day 12 and then restored at the end of each cycle. No malignant findings were observed in the resected specimen. Thus, our results suggest that reduced cisplatin dose can be applied in TPF induction chemotherapy for oral squamous cell carcinoma in patients with a solitary kidney. However, close monitoring for AE is required for patients with a low eGFR, because the relative risk of terminal renal disease becomes 3 to 5 times higher after a unilateral nephrectomy, while the absolute risk remains small [7]. Also, repeated chemotherapy chronically reduces eGFR in a dose-dependent manner [8]. Therefore, a long-term follow-up is essential, and an individualized treatment plan should be established to protect renal function as much as possible against further chemotherapy.

Conclusion

We reported TPF induction chemotherapy for mandibular gingival cancer in a patient with a solitary kidney. Our results suggested that chemotherapy with decreased cisplatin dose can achieve an antineoplastic effect, maintaining renal function in the short term.

healthy kidney pairs [4]. Nevertheless, life-long follow-up should be performed because such patients are at higher risk of urinary tract infection, ischemic/hypoxic renal injury, and exposure to nephrotoxic drugs [5].

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