中文題目：高劑量維他命 C 在一位腎移植併復發性尿路上皮細胞癌患者引起的急性草酸腎病變-病例報告與文獻回顧

英文題目：High-dose vitamin C-induced acute oxalate nephropathy in a renal transplant patient with recurrent urothelial cell carcinoma: a case report and literature review

作　　者：沈宗郁[1]，陳盈妊[2], 王明誠[3], 張勝勛[4]

服務單位：[1]國立成功大學醫學院附設醫院內科部, [2]國立成功大學醫學院附設醫院病理部, [3]國立成功大學醫學院附設醫院腎臟科, [4]國立成功大學醫學院附設醫院移植外科

Introduction: Intravenous injection of vitamin C has been applied in patient with burn, sepsis and malignancy. Ingestion of vitamin C is generally regarded as harmless, but secondary oxalosis induced acute kidney injury had been reported. The risk of oxalate nephropathy seemed to be highest in patients with chronic kidney disease.

Case presentation:

We presented one 41-year-old female case with kidney transplantation who received high-dose vitamin C infusion for recurrent urothelial carcinoma. She received 7 doses of intravenous vitamin C 1000 mg per day administered by a medical practitioner. She developed acute kidney injury and anuria four days later. She remained nearly anuria despite loop diuretics use and aggressivehydration. Her serum creatinine level was 1.7 mg/dL 7 days prior, 7.3 mg/dL on presentation, and peaked at 10.4 mg/dL. Urine sediment examination revealed numerous monohydrated calcium oxalate crystals.She received emergent hemodialysis on the forth day after admission. Renal biopsy on the sixth day after admission revealed diffuse translucent crystals deposition in a background of marked tubular atrophy, interstitial fibrosis and interstitial inflammation on hematoxylin and eosin stain. These crystals showed birefringent on polarized light and distributed within both tubular epithelial cytoplasm and tubular lumen, accompanied with tubular dilatation, consistent with calcium oxalate crystal deposits.The diagnosis of acute oxalate nephropathy was made.

The patient was discharged with dialysis-dependent after four weeks of treatment. Fortunately, her renal function improved gradually and hemodialysis was discontinued 6 months later. Her serum creatinine level was 3.6 mg/dL after cessation

of hemodialysis. We further conducted a literature review to find case reports of vitamin C-induced nephropathy tohighlight the risk factorsfor vitamin C-induced oxalate nephropathy.

Discussion:

Vitamin C therapy in cancer patients has a long history of controversy. Although vitamin C was thought to be well tolerated in previous studies, cases of vitamin C-induced oxalate nephropathy had been reported. Oxalate is the metabolic end-point of vitamin C, and high-dose vitamin C treatment may increase oxalate concentration and urinary oxalate. Oxalate crystals deposition in renal and interstitium will lead to acute tubular necrosis, so called oxalated nephropathy.

On literature review, a total of 31 cases, including our case, with biopsy-proven vitamin C-induced oxalate nephropathy were reported. Considering the administration route, 21 (67.7%) patients received oral vitamin C supplement for nutrition supply (20 cases, 64%) and cancer (one case for uterine leiomyosarcoma, 3%); and 10 (32.2%) patients received parenteral high-dose vitamin C supplement for cancer (2 cases, 6%), sepsis (2 cases, 6%), burn injury (3 cases, 9%), renal amyloidosis (1case, 3%), and nutrition supply (1 case, 3%). The doses varied greatly, while not reported sometimes, at least 500 mg orally per day. Most of the patients (28 cases, 90%) developed acute kidney injury requiring dialysis therapy, only three patients (10%) did not receive hemodialysis. Among those three patients, two patients regained renal function after supportive treatment and discontinuation of vitamin C supplement. One patient did not receive hemodialysis according to his will, and he finally expired due to progressive acidosis. For renal outcome, 17 patients (54.8%) had a full or partial renal recovery and hemodialysis was discontinued, and 14 patients (45.2%) remained dialysis-dependent (8 patients) or died (6 patients, 2 related to discontinuation of hemodialysis).There were 7 renal transplant patients, including the present patient, had biopsy proven vitamin C-induced oxalate nephropathy. Only three of them (42%) were dialysis free at discharge.

We found some potential risk factor for vitamin C-induced oxalate nephropathy, including baseline impaired renal function (eGFR < 60 ml/min/1.73m2), history of kidney transplantation, and parenteral route administration. This finding indicates that, for patients at risk factor for vitamin-C induced oxalate nephropathy, high dose vitamin-C should be used with caution.

Conclusion: We believe that high-dose vitamin C led to the acute oxalate nephropathy in this renal transplant recipient. Considering the weak evidence of vitamin C therapy in cancer therapy, we suggest that high-dose vitamin C therapy should be avoided in patients at risk for vitamin C-induced oxalate nephropathy.