中文題目：在具有腎性腹水和心因性腹水的一位血液透析患者使用aminodarone治療期間發生頑固性腹水

英文題目：Development of Refractory Ascites during Amiodarone Therapy in a Hemodialysis Patient with Nephrogenic ascites and Cardiogenic Ascites

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Backgrounds: The uremic milieu could predispose patients with renal failure to disturbed thyroid function. Furthermore, the disturbed thyroid function in chronic renal failure could be further aggravated by amiodarone.

Materials and Methods: A hemodialysis patient with cardiogenic ascites coincided with nephrogenic ascites and amiodarone- induced hypothyroidism was retrospectively evaluated.

Results: A 65-year-old female patient had a history of tricuspid regurgitation, congestive heart failure, hypertension, left knee fracture s/p operation, acute myocardial infarction, triple vessel disease status after coronary artery bypass surgery, amputation right below knee, and diabetic nephropathy. She was treated with amiodarone for about 1 year to prevent ventricular arrhythmia. The results of laboratory investigations of three episodes of ascitic fluid are shown in Table 1. During the first episode of ascites, the diagnoses based on laboratory examinations were as follows: Non-enhanced computerized tomography demonstrated right-side pleural effusion, moderate ascites, slightly small-sized liver with slightly uneven contour, left renal cyst, some fluid around the portal vessels indicating periportal edema, and no pericardial effusion (Figure 1A and B). Abdominal ultrasound examination revealed hepatic venous congestion. Therapies of cardiogenic ascites with diuretics, inotropic agents, and therapeutic paracentesis were performed. Subsequently, she was admitted because of a second episode of ascites. Results of laboratory investigations were as follows: albumin, 3.5 g/dL (reference value 3.5–5.2 g/dL); blood urea nitrogen, 57.2 mg/dL (reference value 5.0–24.0 mg/dL); creatinine, 4.7 mg/dL (reference value 0.5–1.3 mg/dL). Renal sonography revealed parenchymal renal disease (left side 9.6 cm, right side 9.8 cm). The ascitic fluid urea level was 23.9 mg/dL after approximately 2 months of intensive hemodialysis. A vigorous search for

esophageal varix, splenomegaly, portal vein thrombosis, pericardial disease, peritoneal malignancy, pancreatic pseudocyst, inferior vena cava obstruction, Budd–Chiari syndrome, urinary extravasation, and veno-occlusive disease, including non-enhanced computerized tomography and upper gastrointestinal scope, produced negative results. Hepatitis B surface antigenemia and hepatitis C viral serological markers were negative. In addition to cardiogenic ascites, the patient was believed to be suffering from nephrogenic ascites after exclusion of other causes of exudative ascites. Thus, rigid fluid control, intensive hemodialysis, high-protein diet, and intravenous albumin infusion were performed with the diminution of ascites. Later, refractory ascites occurred. Further laboratory studies produced the following results: The thyroid-stimulating hormone level was 17.8 mIU/L (reference value 0.3–5 mIU/L) with a free T4 (thyroxine) of 1.05 ng/dL (reference value 0.8–2 ng/dL). Antithyroid peroxidase antibody was 22 IU/mL (reference value <35 IU/mL). Antithyroglobulin antibody was <20.0 IU/mL (reference value <40 IU/mL). Thus, occurrence of amiodarone-induced subclinical hypothyroidism appeared to be likely. The follow-up thyroid-stimulating hormone level was 17.6 mIU/L with a free T4 (thyroxin) of 0.56 ng/dL. Thus, treatment with low-dose thyroxine sodium (25 mcg/day) was instituted, leading to diminution of ascites.

Discussions: The uremic milieu could predispose patients with renal failure to disturbed thyroid function. Thyroid function may be directly influenced by many factors in renal failure. Protein caloric malnutrition could directly disturb thyroid function. Fluoride derived from dialysate may also interfere with thyroid function. Uremic toxins could inhibit the peripheral conversion of thyroxine (T4) to triiodothyronine (T3). Uremic toxins may interfere indirectly with thyroid function through pituitary-thyroid axis. Plasma iodide may be increased in the blood of hemodialysis patients and could interfere with thyroid function. When the plasma iodide level is elevated to a critical threshold, acute inhibition of iodine organization and subsequent thyroid hormone synthesis (acute Wolff-Chaikoff effect) occur. Adaptation to large doses of iodide is rapid, occurring in 48 hours, which is linked with auto-regulatory inhibition of iodide transporter across the intrathyroidal membrane. Failure to escape from the Wolff-Chaikoff effect is proposed to account for aminodarone-induced hypothyroidism. Amiodarone is eliminated primarily by hepatic metabolism and biliary excretion. Thus, the pharmacokinetics of amiodarone is not affected by chronic renal failure. The mechanisms of amiodarone-induced hypothyroidism were proposed to be the following: First, amiodarone inhibits the peripheral conversion of thyroxine (T4) to triiodothyronine (T3) by competitive inhibition of 5'-monodeiodinase and favors the generation of reverse T3, which has no T3 activity. Second, amiodarone is an iodinated compound that contains 37.2 % of its

molecular weight as iodide. In our patient, about 9 mg/day of iodide released from dehalogenation of 300 mg of amiodarone. As the daily iodide requirement is about 200 ug, the patient received many times her normal daily requirement.

Chronic renal failure patients with unexplained and refractory ascites and anemia should be tested for hypothyroidism especially during amiodarone therapy. In this patient with a complex pathogenesis of ascites, SAAG can be omitted in the third round of diagnostic abdominal paracentesis. Uremic conditions and long-term therapy of aminodarone could complementarily cause hypothyroidism. We observed that amiodarone-induced hypothyroidism, even in the subclinical stage, could facilitate the accumulation of ascites in the patient. When the ascites of hemodialysis patients becomes refractory, hypothyroidism should be kept in mind. A low-dose T4 sodium was suggested initially for fear of atrial fibrillation.

Conclusion: When hemodialysis patients with nephrogenic ascites and cardiogenic ascites became refractory, we should search hypothyroidism and use low dose thyroxine sodium initially for fear of atrial fibrillation.