中文題目：病例報告 ： 吃檳榔引發之高血鈣症

英文題目：A case report : Betel nut related hypercalcemia

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## Introduction

Chewing betel nuts is common in Far East Asia, India, and the South Pacific islands. There are about 600 million users of betel nuts worldwide.[1] Oral submucosal fibrosis and squamous cell cancer are the most commonly reported harmful effects of betel nut chewing.[2,3] Milk-alkali syndrome is another toxic, but less known effect.[4-6]

## Case Presentation

The 37-year-old man had noted to have type 2 diabetes mellitus, hypertension, and dyslipidemia for 1 year. He received irregular follow-up at our outpatient clinic and took medicine very irregularly. The prescription included metformin 500 mg twice daily, pioglitazone 30 mg once daily, candesartan 8 mg once daily, and fenofibrate 200 mg once daily. He had chewed at least 50 white lime betel nuts wrapped in the leaves of *Piper betle* with ground oyster shell paste daily for more than 10 years. He spat the initial saliva mixed with white lime betel nut paste out one time and swallowed the later saliva.

He complained general malaise and poor appetite for about 1 month this time, along with dizziness and headache. Symptoms got more severe in recent days, even could not work as usual. Furthermore, increased water intake and urine output, and muscle soreness over his shoulder and neck were also mentioned. Therefore, due to above discomforts, he came to our hospital for help. Tracing his history, conscious was clear. He denied fever, nausea, vomiting, abdominal pain, bone pain, nor tea-colored urine. Also denied took any diuretics, herbs and other drugs. After admission, random blood sugar was 108 mg/dl. Serum creatinine was 5.2 mg/dl (his baseline level was around 1.6 mg/dl). Serum calcium was 14.1 mg/dl. Hypercalcemia and acute kidney injury were noted.

Great amount of hydration and furosemide were used for hypercalcemia managements. Serum i-PTH, phosphorus, and 24 hours urine calcium were also send for hypercalcemia survey. However, iPTH was very low (1.0 pg/ml), serum phosphorus was within normal range (3.0 mg/dl), and 24 hours urine calcium was 721 mg. Hyperparathyroidism was not favored, and malignancy related hypercalcemia was under considered. Therefore, serum alpha fetal protein (AFP), Carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA 199), Prostate specific antigen (PSA), and Squamous cell carcinoma antigen (SCC) were send for malignancy survey though

just AFP, CEA, and SCC were mild elevated (AFP: 7.78 ng/ml; CEA: 4.63 ng/ml; SCC: 2.40 ng/ml) while CA 199 and PSA were within normal range. Due to betel nut use history and elevated serum SCC, ENT doctor was consulted though still no specific lesion was found. Abdomen MRI was also arranged, which revealed a hepatic hemangioma at segment VI of liver, and nonspecific cysts and hemangiomas lesion at bilateral kidneys. Panendoscopy and colonscopy were also performed. Colonscopy showed negative finding. Panendoscopy showed multiple white plaques at whole esophagus and multiple gastric ulcers. Biopsy of ulcers was done and pathology also showed negative finding. Bone scan was also arranged but also no obvious lesion was found.

Negative finding of malignancy was found. Therefore, Milk-alkali syndrome was favored, suspected betel nuts related. During hospital course, just hydration and diuretics were used. Serum calcium level decreased to normal range and acute kidney injury also recovered well. This patient was discharged 1 week later.

## Discussions

Milk-alkali syndrome is the third most common cause of in-hospital hypercalcemia, after primary hyperparathyroidism and malignancy, with a prevalence of more than 12% among hospitalized patients with hypercalcemia.[7] The syndrome is a result of ingestion of large amounts of calcium (in excess of 4 grams per day) and absorbable alkali.[8,9] The diagnosis of MAS requires a history of excessive calcium and absorbable alkali ingestion and the triad of hypercalcemia, metabolic alkalosis, and renal insufficiency.[9] Discontinuation of calcium and alkali usually results in resolution of hypercalcemia and alkalosis, but renal function may not recover completely.[8] Intravenous administration of saline solution and loop diuretics can increase the excretion of calcium and alkali.[4]

Betel nut chewing is a rare cause of MAS.[4-6] In other betel nut chewing countries, betel nuts are usually served with tobacco leaves. In Taiwan, however, betel nuts are usually wrapped in the leaves of *Piper betle* with the ground oyster shell paste containing calcium carbonate.[4] To develop MAS, the daily amount of ingested calcium carbonate has been reported to be more than 4 g (1.6 g of elemental calcium).[11,12]

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