

**Milk alkali syndrome with acute renal failure requiring hemodialysis treatment**

## Hemodiyaliz tedavisi gerektiren akut böbrek yetmezlikli süt alkali sendromu olgusu

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Milk alkali syndrome was defined in patients with chronic epigastric pain using calcium containing antacids. The syndrome consists of a triad of hypercalcemia, metabolic alkalosis and acute renal failure following using high doses of calcium containing antacids. The decrease in the frequency of this syndrome with the development of modern ulcer treatment recently started to increase with the consumption of calcium containing medicine for the prevention and treatment of osteoporosis. Milk alkali syndrome may be life threatening because of hypercalcemia and other components. We report here a case with milk alkali syndrome after excessive intake of antacids, presenting with severe hypercalcemia and nonoliguric acute renal failure requiring hemodialysis treatment.

**Key words:** hypercalcemia, milk alkali syndrome, acute renal failure, calcium carbonate.

**Özet**

Süt alkali sendromu kronik epigastrik ağrı nedeniyle kalsiyum içeren antiasid kullanan hastalarda tanımlanmıştır. Sendrom kalsiyum içeren antiasidlerin yüksek dozda kullanılması sonrası gelişen hiperkalsemi, metabolik alkaloz ve akut böbrek yetmezliği üçlemesinden oluşmaktadır. Modern ülser tedavilerinin gelişmesiyle sıklığı azalan sendrom günümüzde osteoporozun önlenmesi ve tedavisi amacıyla kalsiyum içeren ilaçların kullanımı nedeniyle artmaya başlamıştır. Süt alkali sendromu hiperkalsemi ve diğer komponentleriyle hayatı tehdit edici olabilir. Çalışmamızda kalsiyum içeren antiasid ilacın aşırı dozda kullanılması sonrası gelişen şiddetli hiperkalsemi ve diyaliz tedavisi gerektiren nonoligürik akut böbrek yetmezliği ile başvuran süt alkali sendromlu bir olguyu rapor ettik.

**Anahtar kelimeler:** Hiperkalsemi, süt alkali sendromu, akut böbrek yetmezliği, kalsiyum karbonat.

**Introduction**

Although currently rare, milk alkali syndrome (MAS) is one of the important reasons for hypercalcemia. It consists of a triad involving hypercalcemia, acute renal failure and metabolic alkalosis (1-6).

The syndrome can be cured with early diagnosis and proper treatment, but may be life threatening if it is not recognized (4-7).

It may cause irreversible damage such as soft tissue calcifications and chronic renal failure. The primary problem is excessive intake of calcium and absorbable alkalis together with a decrease in renal clearance of these substances.

Replacement of antacids with H2 receptor antagonists and proton pump inhibitors in peptic ulcer therapy

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decreased the frequency of this syndrome in peptic ulcer patients, but increased consumption of calcium containing medicine for prevention and treatment of osteoporosis expanded the population under risk of MAS development. In a study with 100 hypercalcemic patients between 1990-1993, MAS was the third frequent (12%) reason for hypercalcemia following malignancy hypercalcemia and primary hyperparathyroidism (8). Other reasons include excessive calcium intake for osteoporosis, consumption of calcium tablets for chronic renal failure, lymphoma and other granulomatous diseases (9). MAS development requires a 4-60gr daily calcium carbonate intake.

Hypercalcemia causes acute renal failure and metabolic complications with different mechanisms. Polyuria and hypovolemia caused by stimulation of calcium sensitive receptors in the ascending loop of Henle and decreased expression of aquaporins in collecting tubules are included in these mechanisms (10). Hypercalcemia causes renal vasoconstriction in addition to volume loss and results in deterioration of renal function and diminished glomerular filtration rate. Hypercalcemia continuing for longer periods may cause nephrocalcinosis leading to chronic renal failure (11).

MAS is diagnosed with a history of excessive calcium and absorbable alkali intake after excluding other possible reasons for hypercalcemia. A smaller group of patients with hypercalcemia have the components of this syndrome. Kapsner et al. investigated hypercalcemia in 297 cardiac transplant patients undergoing high dose calcium carbonate therapy for prevention of osteoporosis, and 65 of these patients had hypercalcemia while only three of them had milk alkali syndrome. Contributors to development of this syndrome are treatment with thiazide diuretics, vitamin D tablets and chronic renal failure (8).

Treatment of MAS consists of hydration, furosemide, etidronate/pamidronate in eligible patients, hemodialysis and cessation of calcium and contributing factors (5, 12).

### **Case Report**

Our patient was a 50-year old man with hypertension and coronary artery disease. He had symptoms of nausea, vomiting, stomachache, frequent and large volume urination, gastric burning, bloated feeling (in the stomach), pyrosis and decreased oral intake. In the physical examination, his blood pressure was 130/80mmhg, pulse rate 90 beat/minute, respiratory rate 14/minute, body temperature 36,8°C and a cardiac examination revealed a grade 1 systolic murmur. Head and neck, thorax and abdomen examinations were

normal. Oral mucosa was dry, skin turgor and tonus were diminished and there was a slight loss of strength in extremities. Laboratory test results were as follows; BUN:70 mg/dl, Cr:10,3 mg/dl, Ca:17 mg/dl, Na: 139meq/lt, K:4,2 meq/lt, arterial blood Ph:7,5 and HCO<sub>3</sub>:38meq/lt. ECG revealed sinus rhythm and QT interval prolongation. Lung radiography and kidney ultrasonography were normal. He had a history of antacids ingestion 3-4 tablets/day (calcium carbonate 680mg+ 80mg magnesium carbonate) for the previous two years due to dyspeptic symptoms and in the previous month he had used 15-20 tablets/day for increased symptoms. The patient was hospitalized because of hypercalcemia due to excessive calcium carbonate containing antacids, metabolic alkalosis and acute renal failure. The calcium carbonate was stopped; isotonic nacl serum infusion and furosemide therapies were initiated. Other reasons for hypercalcemia (hyperparathyroidism, multiple myeloma, malignancy, sarcoidosis) were excluded. Endoscopy revealed ulcers in the duodenal region and cardioesophageal junction and proton pump inhibitor therapy was started. The patient's clinical and laboratory findings (azotemia, hypercalcemia, etc) did not improve properly and a low-flow rate hemodialysis with low calcium level was initiated. The patient had two sessions of hemodialysis and his general status and symptoms improved in a period of seven days with laboratory values returning to normal ranges.

### **Discussion**

Changes in serum electrolytes may cause various clinic pictures (neurological symptoms, azotemia, and deterioration of general health status). Serum electrolytes, and sometimes urine electrolytes, must be analyzed in patients with these kinds of symptoms and findings. Our patient had MAS consisting of hypercalcemia due to excessive antacid intake, metabolic alkalosis and acute renal failure. Possible other reasons were malignancy, hyperparathyroidism and diuretic use (8).

Severe hypercalcemia is a life threatening state. Prognosis and clinic presentation is associated with length of progression period, calcium level and underlying reasons (9). Our patient had characteristics of acute MAS consisting of hypercalcemia due to excessive intake of calcium containing antacids, metabolic alkalosis, acute renal failure, decreased serum parathormone and normal D vitamin levels. As in our case, all symptoms and findings resolve with cessation of calcium intake in acute MAS. Other possible reasons

for hypercalcemia such as malignancies, multiple myeloma, hyperparathyroidism and sarcoidosis must be excluded (13,14,15). Lung radiography, serum and urine immunoelectrophoresis, albumin/globulin ratio, serum immunoglobulin levels and CT scan and bone scintigraphy of the whole body were normal in our patient. In addition, improvement of the patient's general health status in a short time with treatment for acute MAS also supports the diagnosis. MAS was less frequently seen with widespread use of modern ulcer therapies, but recently MAS cases have tended to increase again with the increased consumption of calcium tablets for osteoporosis treatment and prevention (3).

MAS has three different forms and they may differ in severity. The acute form is characterized by weakness, nausea, vomiting, myalgia and irritability, as in our case. It may cause lethargy and coma if not recognized and treated early. The subacute form may result in band keratopathy and conjunctivitis. In the chronic form, nephrocalcinosis and irreversible renal failure may occur (17).

Rapid improvement of hypercalcemia and the patient's general status with cessation of calcium containing pills is important in the differential diagnosis of MAS. Chronic renal insufficiency may cause MAS with lower doses of calcium. A detailed history including medication use should be obtained for diagnosis. In our patient, a detailed history was obtained regarding possible etiologies. Both exclusion of other possible reasons for hypercalcemia and efficiency of administered therapy support the diagnosis.

Hypercalcemia deteriorates renal functions via dehydration due to polyuria and causes renal

vasoconstriction resulting in decreased glomerular filtration rate (11). Metabolic alkalosis secondary to hypercalcemia is caused by increased bicarbonate absorption from proximal tubules. The reason MAS develops in only a few patients with hypercalcemia is not known, but severity and duration of hypercalcemia, deteriorated renal functions and susceptibility of the patient are predisposing factors (16). Long period exposure to calcium containing antacids and lack of any testing for calcium in our patient in this interval suggests the possibility of long term hypercalcemia. In addition, as the patient has a history of hypertension, he might have renal damage which may facilitate MAS development.

If early diagnosed and properly treated, life threatening hypercalcemia of MAS is rare. Fluid replacement to increase calcium and bicarbonate excretion by furosemide are the main steps of therapy. Magnesium and potassium levels should be tested. Hemodialysis is effective in treatment of patients with severe azotemia and hypercalcemia. It is important to note that clinicians must avoid overtreatment with a risk of hypocalcemia. Because of severe hypercalcemia and renal failure, an intensive therapy including hemodialysis was administered to our patient and we did not face any treatment related complication.

In conclusion, patients with peptic ulcers must be treated with proton pump inhibitors and must avoid excessive intake of antacids. Patients treated with calcium due to different etiologies should be informed about symptoms and findings of hypercalcemia and testing for calcium levels should be performed within appropriate intervals. If MAS develops, proper therapy must be started promptly in order to prevent complications.

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