from urinary tract infection and preventing subsequent renal parenchymal defects is the prompt diagnosis and treatment of the infection. This is particularly important in infants and young children, in whom the diagnosis can easily be missed.

NICE has developed tools to help organisations implement the guidance (see www.nice.org.uk/page.aspx?o=tools).

Contributors: RM was the project manager and systematic reviewer; he drafted the paper, and all authors contributed to its revision and the final draft. ML is the

clinical co-director for the guidelines, was the project director, and convened the Guideline Development Group. KV-J chaired the Guideline Development Group.

Competing interest: None declared.

Funding: The National Collaborating Centre for Women's and Children's Health was commissioned and funded by the National Institute for Health and Clinical Excellence to write this summary.

Provenance and peer review: Commissioned; not externally peer reviewed.

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LESSON OF THE WEEK

Milk alkali syndrome without the milk

Michail Kaklamanos, Petros Perros

Endocrine Unit, Freeman Hospital,
Newcastle upon Tyne
NE7 7DN

Correspondence to: P Perros
petros.perros@ncl.ac.uk

BMJ 2007;335:397-8

doi: 10.1136/bmj.39247.754676.BE

Milk alkali syndrome is easily missed and should be considered in all patients who present with hypercalcaemia

Milk alkali syndrome is the **third commonest cause of hospital admissions for hypercalcaemia**,^{1 2} but the diagnosis is often missed.²⁻⁵ Misdiagnosis can lead to unnecessary and potentially invasive investigations and inappropriate treatment

Case report

A 76 year old woman was referred to a gastroenterology outpatient clinic with altered bowel habit. She had a six month history of alternating constipation and diarrhoea, and she admitted to polydipsia, polyuria, and nocturia. She had no nausea, vomiting, abdominal pain, or weight loss. Her regular prescriptions included salbutamol inhaler, a calcium channel blocker, and ibuprofen for chronic obstructive pulmonary disease, hypertension, and osteoarthritis. She had a history of dyspepsia caused by gastric erosions noted on gastroscopy. She denied taking vitamin supplements or other over the counter medications.

Clinical examination was unremarkable, but routine investigations showed hypercalcaemia (table). She was admitted for immediate treatment with intravenous fluids and intravenous infusion of disodium pamidronate 90 mg. On the second day after admission, her serum calcium concentration was normal. The results of additional investigations taken before disodium pamidronate was started became available later (table). There was no clinical evidence of acidosis, such as Kussmaul's respiration, though we did not test her arterial pH. Results of chest radiography, abdominal computed tomography, bone scan, and mammography were all normal. Her serum calcium concentrations remained normal without further need for disodium pamidronate infusions or intravenous fluids.

After we had treated her hypercalcaemia, careful

Laboratory test results (serum concentrations unless stated otherwise) from patient with milk alkali syndrome

At presentation	Result (normal range)
Calcium (mmol/l)	3.45 (2.25-2.7)
Phosphate (mmol/l)	1.36 (0.8-1.44)
Creatinine (mol/l)	124 (65-120)
Intact parathyroid hormone (ng/l)	8 (5-60)
25 (OH)D3* (nmol/l)	59 (10-50)
Urine calcium/creatinine ratio (mmol)	1.03 (0.0-0.7)
Free thyroxine (pmol/l)	18 (11-23)
Thyroid stimulating hormone (mU/l)	1.76 (0.3-4.7)
Random cortisol (nmol/l)	611
Angiotensin converting enzyme (U/l)	19 (8-52)
Day 2	
Calcium (mmol/l)	2.55 (2.25-2.7)
Creatinine (mol/l)	111 (65-120)
Day 6	
Calcium (mmol/l)	2.35 (2.25-2.7)
Creatinine (mol/l)	94
Three months after discharge from hospital	
Calcium (mmol/l)	2.46 (2.25-2.7)
Creatinine (mol/l)	83 (65-120)
Intact parathyroid hormone (ng/l)	25 (5-60)

*25 hydroxycholecalciferol.

review of her drug history showed that for the previous two years she had been taking six to eight indigestion tablets daily (equal to 5.5 g calcium carbonate a day) to alleviate her dyspepsia. She denied any concomitant consumption of milk or milk products. The patient was advised to discontinue these tablets and the ibuprofen. Her dyspepsia did not recur, and she did not require further gastrointestinal investigations or the introduction of proton pump inhibitors. She was discharged with normal calcium concentrations (2.35 mmol/l) six days after admission. Three months later,

during a scheduled follow-up, results of biochemistry tests remained normal (table).

Discussion

Milk alkali syndrome is a hypercalcaemic disorder initially described in association with excessive consumption of milk and sodium bicarbonate for the treatment of peptic ulcer disease (the Sippy diet).^{3 4 6 7} The syndrome became rare after the introduction of H_2 blockers and proton pump inhibitors in clinical practice. Recent data, however, suggest a rising incidence of milk alkali syndrome as a cause of severe hypercalcaemia, probably as a result of increasing use of medications containing calcium carbonate (mainly dispensed over the counter) and other calcium rich products.^{1 3 4} Two series of 100 and 125 patients have shown that milk alkali syndrome is the third most common cause of hospital admissions for hypercalcaemia.^{1 2} The diagnosis is based on a history of ingestion of calcium rich compounds, concordant biochemical findings, and exclusion of other causes, the commonest being primary hyperparathyroidism (associated with an raised serum parathormone) and hypercalcaemia of malignancy (hence the screening tests for malignancy). Rarer causes of hypercalcaemia include thyrotoxicosis (excluded by normal serum thyroid stimulating hormone), Addison's disease (excluded by a high normal serum cortisol concentration) and sarcoidosis (unlikely in view of the normal results for angiotensin converting enzyme).

Milk alkali syndrome should be considered in all patients who present with hypercalcaemia. Preparations that contain calcium carbonate are widely used for many medical conditions, including simple dyspepsia, renal failure (as phosphate binding agents), and prophylaxis or treatment of osteoporosis. The key element to the development of milk alkali syndrome is an increased calcium intake, which is also responsible for the development of metabolic alkalosis and renal failure. The presence of the two latter features defines the advanced form of milk alkali syndrome and progression to it depends on several factors, including individual differences in intestinal absorption of calcium, old age, decreased gastric pH, and pre-existing renal failure. The daily amount of ingested calcium plays an important role in the pathogenesis of milk alkali syndrome, with quantities ranging from 2-15 g

calcium carbonate a day being implicated.^{3 6-9}

Early diagnosis and treatment of hypercalcaemia is associated with a favourable outcome.^{3 7 8} Altered mental status caused by hypercalcaemia at the time of presentation may affect the accuracy of the history from the patient and pose an obstacle to timely diagnosis and management. A careful history of drug use should always be taken from patients who present with hypercalcaemia and corroborated by relatives, carers, or the patient's primary care physician. The management of milk alkali syndrome is withdrawal of the offending medications and correction of volume depletion with or without calciuresis. Although bisphosphonates have been used, they should be avoided as the above measures are usually effective, increased bone resorption is not thought to play a important pathogenetic role, and hypocalcaemia can result from bisphosphonate use.⁵

Given that calcium carbonate has replaced milk products as the main source of calcium leading to the syndrome, we suggest that "calcium alkali syndrome" is a more appropriate name.

Contributors: MK wrote the manuscript and followed the patient's progress after her discharge from hospital. PP made the diagnosis, was responsible for managing the patient, reviewed the case report, and is guarantor.

Funding: None.

Competing interests: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Can you say "no"?

The distance between yes and no is the same as that between slavery and freedom. I left a third world country to come to the UK thinking that I had jumped over the barrier between yes and no, leaving slavery behind.

Early in my career as a trainee in histopathology, I was reporting a case of a basal cell carcinoma with my consultant. His instructions were to report the case according to the standards of the minimum dataset of the Royal College of Pathologists. This includes mentioning whether there is perineural invasion and lymphovascular invasion. I am not convinced that this is needed in all cases. Perineural invasion is rare and seen

usually with only one type of basal cell carcinoma. The lymphovascular invasion is even rarer, if it occurs at all.

I mentioned this to my consultant, who said I was correct but that, as long as these criteria were on the dataset, we had to fulfil them.

"Why?" I protested.

"Because this is what the college wants us to do."

"What if we do not see a point of this?"

"I agree with you, Heyam, but we still cannot say 'no.'"

What a surprise. Wherever I go, wherever I live, "no" is still a difficult word to say.

Heyam Awad consultant, Tameside NHS Trust, Manchester
heyamawad2000@yahoo.com