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MEDICAL GRAND ROUNDS

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INTERRELATIONS BETWEEN CALCIUM AND SODIUM METABOLISM

Case 1: ([redacted])

This 39 year old [redacted] man was in excellent health until 10 days before admission. At that time he developed nausea and vomiting, for which he took castor oil. This resulted in severe diarrhea. He was admitted to another hospital on [redacted] 1969. He was transferred to [redacted] on [redacted] 1969 for treatment of renal failure. On admission he appeared to be severely salt-depleted with poor skin turgor, orthostatic hypotension and tachycardia. He remained in the hospital for 10 days during which time the salt depletion was partially corrected. There was some clinical improvement but he continued to have poor appetite, ate little, and vomited intermittently.

On [redacted] 1969 he left the hospital AMA. He continued to vomit while out of the hospital and returned for readmission on [redacted] 1969. During this 14-day interval his weight decreased from 205 to 189 lbs. On physical exam he again appeared to be severely salt depleted and had orthostatic hypotension.

Laboratory data:

Date	[redacted]-69	[redacted]	[redacted]	[redacted]	Prednisone 100 mg daily ([redacted]	[redacted]	[redacted]	[redacted]	[redacted]
BUN	108	141	23	60	51	30	15	9	16
Creatinine	9.1	12.6	2.2	6.5	4.8	0.9	1.6	1.5	1.5
Uric Acid	12	17	7.6	13.0	10.7	6.5	6.3	9.4	9.0
Serum prot.	8	6.4	---	8.0	----	---	8.1	---	8.2
Alb.	3.4	3.3	---	3.8	----	---	4.0	---	---
Glob.	2.0	1.5	---	2.2	----	---	1.3	---	---
mg%	14.2	12.2	12.9	14	12.8	8.2	9.3	10.6	10.4
P mg%	----	3.0	3.6	5.5	4.5	2.1	5.0	4.3	3.8

Other data:

Hemoglobin was 14 gm% initially, and fell to 11.2 gm% after rehydration. Serum Na - 120 mEq/L, K - 5.3 mEq/L, CO_2 content 18 mEq/L, FBS 120 mg%, serum amylase <320 units, plasma cortisol 7 ugm% at 4:00 p.m., alk. phosphatase 9.5 K.A. units, calcium excretion 103 mg/day, GFR - 70 ml/min., Bence-Jones protein neg., L.E. prep - negative, all skin tests negative. Bone marrow - granulocytic hyperplasia, liver biopsy - normal, bone films - normal. Upper G.I. series - normal.

Additional retrospective history:

Increased milk intake and ingestion of Rolaids for two months prior to admission. Denied taking any antacids containing calcium.

Conclusions:

Severe salt depletion, hyperuricemia, hypercalcemia and pre-renal azotemia. Lymphoma, multiple myeloma, sarcoidosis, hyperparathyroidism were all considered : none could be proved.

Case 2:

This 43 year old [redacted] man was admitted to the surgical service of the [redacted] for evaluation for peptic ulcer and possible pyloric obstruction. Midepigastric pain had occurred intermittently for the previous 6 months, usually after missing a meal and occasionally at night. The pain was relieved by food or milk. He had always been a heavy milk drinker, but during the 4 months preceding admission his milk intake was approximately 1 gallon per day. He denied taking any antacid preparations other than occasional baking soda. He was admitted to the hospital after one week of intractable vomiting.

On admission pulse was 100 and BP 105/70 while supine. Upon standing pulse rose to 132 and BP fell to 90/55. Skin turgor was diminished. During the first f r days he re_ceived approximately 8 L saline and 300 mEq KCl. After rehydration pulse was 76 and BP 125/75 without orthostatic hypotension.

Laboratory results:

spital Day	Hematocrit %	BUN mg%	Na mEq/L	K mEq/L	CO_2 mEq/L	Ca mg%	P mg%
Admission	60	37	129	2.6	36	13.5	3
2	52	25	136	3.3	30	12.8	
4	48	17	142	4.2	27	9.4	4
8	46		138	3.8	28	9.2	3.5

Serial urine calcium excretions were all less than 120 mg/day.

Conclusions:

Transient hypercalcemia in a severely salt-depleted man which was corrected by isotonic saline. May represent the acute form of the milk alakli syndrome.

Case 3:

This 36 year old [redacted] man was admitted to a [redacted] [redacted] hospital in [redacted] 1969 with a documented myocardial infraction. He was placed on a low-salt diet and thiazide diuretics for mild hypertension. He was found to have stag-horn calculus in the left kidney and small, poorly functioning right kidney. While on a low-salt diet and thiazides serum calciums were found to be persistently elevated (12-13 mg%). There was a history of one episode of renal colic two years previously.

He was admitted to [redacted] [redacted] for evaluation in [redacted] 1969. He had voluntarily discontinued the thiazides and low-salt diet after leaving the [redacted]. While at [redacted] serum calciums were normal (8.3 - 10.6 mg%), urine calcium excretion was 225 to 256 mg/day on normal diet and bone X-rays showed no evidence of hyperparathyroidism.

Conclusion:

Thiazide-induced hypercalcemia in a man who has a stag-horn calculus and may have some underlying disturbance in calcium metabolism.

REFERENCES

I. Effect of sodium intake and extracellular volume on calcium excretion.

1. Walser, M. Calcium clearance as a function of sodium clearance in the dog. Am. J. Physiol. 200:1099-1104, 1961.

   Osmotic diuretics and saline infusions produce parallel increments in calcium and sodium excretion.

2. Blythe, W.B., H.J. Gitelman, and L.G. Welt. The effect of expansion of the extracellular space on the rate of urinary calcium excretion. Clin. Res. 14:372, 1966.

   Expansion of extracellular space with isotonic saline in dogs with lowered GFR (aortic constriction) and constant mineralocorticoid increases calcium and sodium excretion proportionately.

3. Kleeman,C.R., J. Bohannan, D. Bernstein, S. Ling and M.M. Maxwell. Effect of variations in sodium intake on calcium excretion in normal humans. Proc. Soc. Exptl. Biol. Med. 115:29-32, 1964.

   Raising sodium intake increases calcium excretion. This can be partially prevented by administration of 9 α -fluorohydrocortisone.

4. King, J.S., R. Jackson, and B. Ashe. Relation of sodium intake to urinary calcium excretion. Invest. Urol. 1:555-560, 1964.

5. Birge, S.J., and L.V. Avioli. Isolation and characterization of an inhibitor of intestinal calcium transport in the dog following expansion of the extracellular space. Clin. Res. 17:424, 1969.

   Expansion of extracellular space with isotonic saline decreased intestinal absorption of calcium in dogs with perfused intestinal loops.

II. Effect of adrenal steroids on calcium excretion.

6. Pedersen, K.O. Hypercalcemia in Addison's disease. Acta Med. Scand. 181:691-698, 1967.

   Two patients with adrenal insufficiency had hypercalcemia (12-15 mg%) and marked hypercalciuria. Administration of cortisone promptly decreased both serum and urine calcium.

7. Walser, M., B.H.B. Robinson, and J.W. Duckett. The hypercalcemia of adrenal insufficiency. J. Clin. Invest. 42:456-465, 1963.

   Hypercalcemia is a common feature of adrenal insufficiency. Total calcium increased, but ionized calcium was normal. Contributing factors were: 1) elevated protein concentrations secondary to hemoconcentration; 2) increased protein binding affinity secondary to hyponatremia; 3) increased filtrable complexes, such as calcium citrate; and 4) increased non-filtrable compound of calcium and phosphate.

8. Suki, W.N., R.S. Schwettman, F.C. Rector, Jr., and D.W. Seldin. Effect of chronic mineralocorticoid administration on calcium excretion in the rat. Amer. J. Physiol. 215:71-74, 1968.

Nine α -fluorohydrocortisone causes transient salt retention and expansion of extracellular volume. Calcium excretion is increased secondary to suppression of proximal reabsorption.

III. Effect of hypercalcemia on tubular reabsorption of sodium.

9. Levitt, M.F., M.H. Halpern, D.A. Polimeros, A.V. Sweet, and D. Gribetz. The effect of abrupt changes in plasma calcium concentration on renal function and electrolyte excretion in man and monkey. J. Clin. Invest. 37:294-304, 1958.

   Hypercalcemia increases excretion of salt and water. May cause salt depletion and dehydration.

10. Massry, S.G., J.W. Coburn, L.W. Chapman, and C.R. Kleeman. Role of serum Ca, parathyroid hormone and NaCl infusion on renal Ca and Na clearances. Am. J. Physiol. 214:1403-1409, 1968.

    1) The normal interdependence between clearance of calcium and sodium is influenced by parathyroid hormone. 2) calcium infusions depress tubular reabsorption of sodium.

11. Suki, W.N., G. Eknoyan, F.C. Rector, Jr., and D.W. Seldin. The renal diluting and concentrating mechanism in hypercalcemia. Nephron 6:50-61, 1969.

    Hypercalcemia inhibits sodium reabsorption primarily in loop of Henle, impairing the renal concentrating and diluting capacity.

IV. Effect of thiazide diuretics

12. Nassim, J.R., and B.A. Higgins. Control of idiopathic hypercalciuria. Brit. Med. J. 1:675-681, 1965.

    Thiazides decrease calcium excretion 30 to 50% in patients with idiopathic hypercalciuria. There was no change in fecal excretion of calcium. Serum calcium was not altered.

13. Yendt, E.R., R.J.A. Gagne, and M.Cohanim. The effect of thiazides in idiopathic hypercalciuria. Am. J. Med. Sci. 257:449-460, 1966.

    In idiopathic hypercalciuria thiazides decrease urine and fecal calcium excretion, causing positive calcium balance and slight increase in serum calcium.

14. Torsti, P., and B.A. Lamberg. The effect of a two-day treatment with chlorothiazide on the urinary excretion of calcium, phosphate and sodium in hyper- and hypocalcemia. Acta Med. Scand. Suppl. 412: 181-191, 1964.

    Thiazides decrease calcium excretion 30 to 40%. Rise in serum calcium is directly proportional to initial serum calcium level.

15. Lamberg, B.A., and Torsti, P. The dependence of calcium excretion on adrenal steroids. Acta Med. Scand. Suppl. 412:193-203, 1964.

Thiazides decrease calcium excretion in normal subjects but not in patients with adrenal insufficiency.

16. Winnacker, J.L., C.G. Duarte, K.L. Becker, and A. Pace. Thiazide-induced hypercalcemia. Clin. Res. 16:277, 1968.

Thiazides increased total calcium but did not change ultrafiltrable calcium. Increased bound calcium related to salt depletion, increased total protein concentration and possibly increased protein-binding affinity.

17. Parfitt, A.M. Chlorothiazide-induced hypercalcemia in juvenile osteoporosis and hyperparathyroidism. New Eng. J. Med. 281:55-59, 1969.

Thiazides produced symptomatic hypercalcemia in osteoporatic children receiving vitamin D and exacerbated the pre-existing hypercalcemia of hyperparathyroidism. Symptoms suggest increased ionized calcium.

18. Paloyan, E., M. Forland, and J.R. Pickleman. Hyperparathyroidism coexisting with hypertension and prolonged thiazide administration. J.A.M.A. 210:1243-1245, 1969.

Six hypertensive patients treated thiazides chronically developed hypercalcemia and were found to have either parathyroid adenoma or hyperplasia at surgery.

19. Koppel, M.H., J.H. Shinaburger, S.G. Massry, M.M. Popovtzer, and J.W. Coburn. Hypercalcemic response to hydrochlorothiazide in uremia. Clin. Res. 17:435, 1969.

Thiazides produced hypercalcemia in dialyzed patients without renal function. Suggests that thiazides either stimulate the release of parathormone from hyperplastic glands or enhance the osseous response to parathormone.

20. Pickleman, J.R., F.H. Straus, M. Forland and E. Paloyan. Thiazide-induced parathyroid stimulation. Metabolism 18:867-873, 1969.

Thiazides caused hypercalcemia and hypophosphatemia in dogs. Serum calcium gradually returned to normal levels. Parathyroid glands appeared hyperplastic on histologic examination.

V. Milk alkali syndrome.

21. Randall, R.E., M.B. Strauss, and W.F. McNeely. The milk alkali syndrome. Arch. Int. Med. 107:163-181, 1961.

Two forms of milk alkali syndrome. Chronic form has hypercalciuria and low-grade hypercalcemia. Acute form is usually precipitated by vomiting and salt depletion: characterized by reversible renal failur alkalosis, hypercalcemia and absence of hypercalciuria.