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BRIEF REPORT

Invited Manuscript Poster on Renal-Related Education American Society of Nephrology, Nov. 16–21, 2010

Nephrology Teaching Tool: Anagrams

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Abstract

At our institution we have developed unique ways of teaching nephrology and attracting medical students and residents to the field of nephrology. One of the ways we have achieved this is doing talks and sessions using puzzles. This teaching tool was designed to enhance resident learning and to complement resident's role as a teacher, while they were on their nephrology elective. Here we present a sample "anagram" and how it was used to teach the medical residents.

Keywords: Anagrams, teaching nephrology, hypercalcemia

INTRODUCTION

Ongoing research and development and an ever-expanding literature in nephrology make it hard to present all concepts about a topic in an article or a textbook chapter. Trainees including medical students and residents have found it hard to keep up with intellectual challenges posed by spectrum of diseases (complex acid–base disorders, fluid and electrolyte balance, etc.) covered under nephrology. Compounded with demanding lifestyle and lower compensation, many have been dissuaded from pursuing this specialty. This has been recognized by nephrology community and has been gaining more attention at recent meetings at American Society of Nephrology. It would be prudent to act now and rediscover new ways to attract residents and students to this field.

At our institution we have recently developed many new ways to teach nephrology to stimulate residents' interest toward this specialty.[1] Among crossword puzzles,[2] concept maps, "role playing," nephrology-related blogging, we have also developed this fun teaching tool called nephrology anagrams.[3] This teaching tool was designed to enhance resident learning and to complement residents' role as a teacher, while they were on their nephrology elective. An anagram is type of word play—a set of jumbled letters, which can be rearranged to find a hidden answer (original word/phrase). For example, "My Car (1 word)" is an anagram for "Camry." A sample anagram is presented here that was created by the resident on hypercalcemia. The anagrams below bring to the reader's attention some of the important things to consider while obtaining a history, physical exam, and laboratory data in the evaluation of hypercalcemia with special reference to calcium, phosphorus, and vitamin D metabolism. Each anagram below is followed by a "hint" meant to intellectually direct the reader toward the correct answer. The number of words that would form the final answer is indicated in parenthesis next to the anagram.

After the resident created these anagrams and hints, they were presented to a group of nephrology fellows and consultants in a conference. The group was given an opportunity to solve this quiz and the resident (with the help of supervising faculty and fellow) who wrote puzzle discussed answers with their

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explanations subsequently. All those who participated were given the opportunity to add information that they may know about the topic, further expanding the knowledge of everyone present. This allows everyone, including the presenters, the chance to learn through interactive methods. This innovative approach to learning/brainstorming further sparks the residents' interest in the topic and toward nephrology. While it is not meant to replace the "traditional" ways of classroom teaching; it allowed the residents and fellows to fill in gaps of knowledge in a fun-involving/interactive way and encourage self-directed learning.

ANAGRAMS

1. HI MULTI (1 word)
   Hint: This drug can cause hypercalcemia. It was first used in the nineteenth century as a treatment for gout but was found that it would break up urate crystals only when it reached toxic levels.
2. A LYMPHOCYTE PRONE ASTHMA (3 words)
   Hint: A 70-year-old man is admitted after a fall and is found to have hypercalcemia and anemia. An X-ray of his head is significant for lytic bone lesions. This is the most common form of renal injury associated with the disease in suspicion.
3. SO TOXIC HISTORY (1 word)
   Hint: A 63-year-old woman presents to your office with weakness, loss of appetite, and weight loss for 6–8 months. Her review of systems is remarkable for constipation and nausea. Her blood work reveals calcium level of 13.5 mg/dL. She is referred to endocrine department for further evaluation of her underlying disease.
4. NOT A CLINIC (1 word)
   Hint: A 73-year-old male suffering from multiple myeloma presents to emergency with confusion, lethargy and polyuria. His labs reveal a serum sodium 148 mEq/L, potassium 3.2 mEq/L, serum bicarbonate 26 mEq/L, blood urea nitrogen 29 mg/dL, creatinine 2.8 mg/dL, calcium 14.5 mg/dL, and glucose 92 mg/dL. Urine osmolality is 150 mOsm/kg. Ct head is negative. This medicine is likely to correct the hypercalcemia most rapidly.
5. CLUB OR SUITES (1 word)
   Hint: A 55-year-old male (originally from India) presented with low-grade fever, generalized weakness, weight loss, abdominal distension and constipation for 4 months. Laboratory workup showed mild anemia with a hemoglobin level of 10.8 gm/dL, white blood cell count of $9 \times 10^3/\mu L$, albumin of 2.4 gm/dL, and hypercalcemia of 12 mg/dL with normal parathyroid hormone level (PTH) of 19.7 pg/mL. What is your diagnosis?
6. BOYS MOLDY HAIRS (1 word)
   Hint: An 83-year-old man is admitted after he passed out in his bathroom onto the floor. He was found 36 h later. He was admitted to the hospital and treated for his acute kidney injury. His labs after 24 h of treatment revealed hypercalcemia with hyperkalemia and hyperphosphatemia.
7. YUCKIER CAKE IMYTATE GUACAMOLE (3 words)
   Hint: A 32-year-old man without significant past medical history presents with fever and epistaxis. On admission, his CBC was significant for white blood cell count of $39 \times 10^3/\mu L$, hemoglobin of 11 gm/dL, and platelet count $29 \times 10^3/\mu L$ with over 30% blasts in peripheral smear. He has normal renal function, calcium of 11.5 mg/dL, an elevated alkaline phosphatase, and lactate dehydrogenase.
8. MAYO DENIES ABIDANCES (3 words)
   Hint: A 70-year-old male with type II diabetes mellitus on hemodialysis for 4 years is admitted after he fell down and found to have a hip fracture. Medications include atenolol, simvastatin, sitagliptin, metformin, calcium acetate (two with meals), and doxercalciferol with dialysis. Labs on admission reveal sodium 132 mEq/L, potassium 4.2 mEq/L, blood urea nitrogen 67 mg/dL, creatinine 6.7 mg/dL, glucose 265 mg/dL, calcium 10.8 mg/dL, phosphorus 5.3 mg/dL, and PTH level of 85 pg/mL. The result of bone biopsy is likely to show this.
9. MODERN SONG FLYERS (2 words)
   Hint: A 22-year-old female presents to emergency with cough, fever, bilateral knee pain, and a painful rash on both lower extremities, progressive over past 5 days. On further questioning, although she is "content with recent weight loss"; she reports having more than usual fatigue on her "routine exercise." On her labs she has calcium level of 11.2 mg/dL. She is also found to have an abnormal chest X-ray and to support his suspicion for this disease, the physician sends the blood for determining angiotensin-converting enzyme levels.
10. TOP TECH PIC (2 words)
    Hint: A 70-year-old male with recently diagnosed lung cancer with metastasis to liver is admitted with confusion and lethargy and found to have a calcium level of 15 mg/dL. PTH is elevated at 509 pg/mL. CT scan of head and neck and bone scan are normal. Total parathyroidectomy is performed and tissue is found to be histologically normal and benign.
11. ADMIRALS KILL MONKEY (3 words)
    Hint: A 32-year-old pregnant woman in her second trimester presents with severe nausea and vomiting. Her labs are remarkable for serum calcium level of 19 mg/dL, alkalosis, and acute renal insufficiency. She reports having a difficult pregnancy with a lot of reflux for which she has been using some over the counter medications.
12. FAMOUS IDIOT SLEUTH (2 words)
    Hint: A 30-year-old male with end-stage kidney

disease presents with lesions on his buttocks and thighs that progressed from painful subcutaneous nodules to black necrotic-looking ulcers. In addition to aggressive dialysis, this adjunctive therapy might benefit.

13. IMMUNE GAS (1 word)
    Hint: Deficiency of above leads to refractory/difficult to correct hypocalcemia.
14. MORONS DINE FANCY (2 words)
    Hint: A 68-year-old male presents to emergency with increasing weakness, dyspnea, and low-grade fever which are intermittent and progressive over past couple of months. His recent onset polyuria and exhaustion led him to the emergency. Labs reveal sodium 144 mEq/L, potassium 3.0 mEq/L, chloride 112 mEq/L, bicarbonate 19 mEq/L, BUN 25 mg/dL, creatinine 1.7 mg/dL, glucose 105 mg/dL, phosphorus 1.9 mg/dL, and calcium 10.8 mg/dL. CBC reveal white blood cell count 15 $\times$ 103/μL and hemoglobin—9.8 g/dL. U/A reveal proteinuria and glycosuria with 2–5 white cells/hpf.
15. HOMBRE DUNNO SYNERGY (3 words) Hint: Hypocalcemia and hypophosphatemia in a 52-year-old female after undergoing total thyroidectomy for bilateral papillary thyroid carcinoma.

ANSWERS

1. Lithium—This drug, now commonly used as a mood stabilizer, can cause hypercalcemia. Lithium competitively inhibits calcium transport across cell membranes thereby blocking calcium influx into cells. It also increases the threshold for the calcium-sensing receptors in the parathyroid glands.[4] This prevents PTH from being shut off when adequate serum calcium levels are met. The intracellular messenger inositol monophosphate is required for interaction between intracellular calcium and nuclear calcium sensor receptors which then regulate PTH hormone gene transcription. Lithium causes a decrease in inositol monophosphate such that the genes for PTH will continue to be transcribed. Lithium may also cause the overproduction of PTH by inhibiting the action of a protein named glycogen synthase kinase 3b—a direct inhibitor of PTH gene transcription.
2. Myeloma cast nephropathy—It is the most common diagnosis among patients with multiple myeloma and clinical renal involvement, accounting for 40–60% of the cases.[5] Other form of kidney diseases associated with multiple myeloma are (a) glomerular—amyloidosis, light and heavy chain deposition disease alone or in combination, and rarely cryoglobulinemia and proliferative glomerulonephritis; (b) tubular—cast nephropathy, crystal globunemia, acute tubular necrosis, proximal and distal renal tubular acidosis, and acquired Fanconi's syndrome; (c) interstitial nephritis and plasma cell infiltration of kidneys.
3. Thyrotoxicosis—Thyroid hormones that are released during times of stress and also for homeostasis. These hormones increase bone resorption leading to the mild hypercalcemia thereby inhibiting PTH secretion and the conversion of calcidiol to calcitriol.[6] These changes can result in impaired calcium absorption and an increase in urinary calcium excretion resulting in osteoporosis and an increased fracture risk. It can be seen in 15–20% of patients with thyrotoxicosis.
4. Calcitonin—Persistent hypercalcemia above 11 mg/dL (2.75 mmol/L) can cause nephrogenic diabetes insipidus.[7] This defect may be associated with reductions both in sodium chloride reabsorption in the thick ascending limb of the loop of Henle, thereby interfering with the countercurrent mechanism, and in the ability of ADH to increase collecting tubule water permeability. Nephrogenic diabetes insipidus due to hypercalcemia may resolve if serum calcium concentrations are corrected. Calcitonin would be the fastest-acting drug for hypercalcemia as it directly inhibits osteoclastic-mediated bone resorption and also increases excretion of calcium and phosphorus by decreasing tubular reabsorption. It can also be given in the state of acute kidney injury when bisphosphonates should be avoided.
5. Tuberculosis—In patients with tuberculosis (TB), hypercalcemia is usually mild and asymptomatic.[8] It may occur in all forms of TB—both pulmonary and extra pulmonary. There is evidence that extra renal 1-α hydroxylation of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol brought about by macrophages plays an important role in causing hypercalcemia in a patient suffering with TB. It is thought that 1,25-dihydroxycholecalciferol can improve the capacity of activated macrophages to kill mycobacteria. This activity usually has local effects to enhance all cell-mediated immunity to TB. However, if produced in a large quantity, spillage may occur into circulation resulting in hypercalcemia.
6. Rhabdomyolysis—In acute kidney injury caused by rhabdomyolysis, the recovery phase may be associated with hypercalcemia and hyperphosphatemia.[9] Hypercalcemia is primarily due to the mobilization of calcium that had been deposited in the injured muscle. Other contributors to elevated calcium levels are correction of hyperphosphatemia (induced by the rise in glomerular filtration rate), mild secondary hyperparathyroidism induced by the renal failure, and an unexplained increase in serum calcitriol concentrations.
7. Acute megakaryocytic leukemia—This condition is part of the acute myeloid leukemia (AML) line of disorders. Specifically this condition is AML FAB

(French–American–British) M7. Hypercalcemia is associated with both lymphoma and leukemia. The etiology of hypercalcemia in myeloid malignancy is poorly defined. This particular case may represent someone with hypercalcemia-attributed bone degradation caused by leukemic cells.[10] It is possible that there is an overproduction of PTH by myeloid cells. PTHrP and increased levels of 1,25-dihydroxyvitamin D3 have been seen to cause hypercalcemia in those with idiopathic myelofibrosis.

8. Adynamic bone disease—It is a common complication seen in patients on dialysis characterized by low osteoblastic and osteoclastic activity (low bone turnover) and is related to excessive suppression of the parathyroid gland due to the administration of calcium-containing phosphate binders and vitamin D analogs. Risk factors include increased age and diabetes. These patients typically have a low serum intact PTH concentration (e.g., <150 pg/mL), which is frequently accompanied by an elevated serum calcium. Many patients are asymptomatic while incidence of hip fractures in this population is estimated to be about 15 times that of general population.[11] Treatment involves discontinuation of calcium-based phosphate binders and vitamin D supplements during dialysis.
9. Lofgren's syndrome—It is included in spectrum sarcoid arthropathy and characterized by the triad of hilar adenopathy, acute polyarthritis, and erythema nodosum. Its pathogenesis is unclear but it is strongly associated with the presence of HLA-DQB1*0201 and specific polymorphisms of C–C chemokine receptor 2. It is usually self-limiting: the erythema nodosum typically disappears in a few months, but the joint symptoms and lymphadenopathy may persist for a of couple years. Angiotensin-converting enzyme levels are elevated in about 15% of these patients who tend to have persistent arthropathy.[12]
10. Ectopic PTH—Ectopic PTH production should be in the differential diagnosis of a patient presenting with malignancy, hypercalcemia, and high level of PTH. In this case, the benign histology of parathyroid tissue after resection in spite of elevated calcium and PTH levels confirm the presence of ectopic production. It has been described in small and squamous cell lung cancer, ovarian cancer, neuroectodermal tumor, and papillary thyroid cancer.[13]
11. Milk alkali syndrome—It is the third most common cause of hypercalcemia in hospitalized patients. Pregnant women are more susceptible to develop this as a result of hyperemesis leading to volume depletion and prolactin-mediated increased calcium absorption through the gut. The pathogenesis is complex and in addition to absorption through gut of high amounts of calcium and alkali, multiple renal mechanisms contribute. Hypercalcemia causes renal vasoconstriction leading to decrease in glomerular filtration and reduced filtered calcium. Also, high affinity of calcium to calcium-sensing receptor on basolateral side of thick ascending loop of Henle leads to sodium wasting and volume depletion which stimulates more calcium absorption in proximal tubule along with bicarbonate. Main therapy is to hold calcium ingestion and volume expand with saline.[14]
12. Sodium thiosulfate—Calciphylaxis is typically characterized by areas of excruciatingly painful ischemic skin necrosis resulting from systemic medial calcification of the arterioles. Hyperparathyroidism, active vitamin D administration, hyperphosphatemia, and an elevated plasma calcium $\times$ phosphate product (Ca $\times$ P), have been implicated in its genesis. Deficiency of inhibitors of vascular calcification like Fetuin-A, which help clear excess calcium and phosphorus from circulation has been postulated. In addition to aggressive dialysis to lower calcium phosphorus product, sodium thiosulfate has also been used.[15] The probable mechanism of action is dissolution of insoluble calcium salts embedded in tissue into soluble calcium thiosulfate. Also, its antioxidant properties may restore endothelial function and promote vasodilation.
13. Magnesium—The most classical sign of severe hypomagnesemia (less than 1.0 mEq/L, 0.5 mmol/L, or 1.2 mg/dL) is hypocalcemia. In addition to decreased PTH secretion, hypomagnesemia also leads to PTH resistance at the level of bone due to reduced cyclic adenosine monophosphate (AMP)-mediated bone resorption.[16]
14. Fanconi syndrome—The patient in this question likely has acquired form of Fanconi syndrome from his multiple myeloma. In some patients, the excess filtered and partially digested light chains interact with apical membrane transport leading to diminished reabsorption of solutes by the proximal tubule which leads to urinary wasting of amino acids, glucose, phosphorus, uric acid, and bicarbonate leading to non-anion gap acidosis, hypophosphatemia, renal glucosuria (glucosuria with a normal plasma glucose concentration), hypouricemia and aminoaciduria.[17]
15. Hungry bone syndrome—This is an important complication in patients with end-stage kidney disease who undergo parathyroidectomy for secondary hyperparathyroidism. In the high turnover state associated with hyperparathyroidism, PTH increases bone formation and resorption with a net efflux of calcium from bone. Sudden withdrawal of PTH in such patients causes an imbalance between osteoblast-mediated bone formation and

osteoclast-mediated bone resorption leading to a marked net increase in bone uptake of calcium, phosphate, and magnesium.[18]

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REFERENCES

[1] Calderon K, Vij R, Mattana J, Jhaveri KD. Innovative teaching tools in nephrology. *Kidney Int.* 2011;79(8):797–799.

[2] Sethi SK, Jhaveri KD. Nephrology crossword: Pediatric nephrology-genetic disorders. *Kidney Int*. 2011;79(11): 1263–1264.

[3] Chawla A, Jhaveri KD. Hypokalemia anagrams. *Am J Kidney Dis*. 2011;57(3):A25–A28.

[4] Haden ST, Stoll AL, McCormick S, Scott J, Fuleihan GEl-H. Alterations in parathyroid dynamics in lithium-treated subjects. *J Clin Endocrinol Metab.* 1997;82(9): 2844–2848.

[5] Pasquali S, Zucchelli P, Casanova S, et al. Renal histological lesions and clinical syndromes in multiple myeloma. Renal immunopathology group. *Clin Nephrol.* 1987;27(5): 222–228.

[6] Richards AJ. Hypercalcemia in thyrotoxicosis with and without hyperparathyroidism. *Postgrad Med J*. 1970;46(537): 440–446.

[7] Garofeanu CG, Weir M, Rosas-Arellano MP, Henson G, Garg AX, Clark WF. Causes of reversible nephrogenic diabetes insipidus: A systematic review. *Am J Kidney Dis*. 2005;45(4):626–637.

[8] Pruitt B, Onarecker C, Coniglione T. Hypercalcemic crisis in a patient with pulmonary tuberculosis. *J Okla State Med Assoc*. 1995;88(12):518–520.

[9] Llach F, Felsenfeld AJ, Haussler MR. The pathophysiology of altered calcium metabolism in rhabdomyolysis-induced acute renal failure. Interactions of parathyroid hormone, 25-hydroxycholecalciferol, and 1,25-dihydroxycholecalciferol. *N Engl J Med.* 1981;305(3):117–123.

[10] Muler JH, Valdez R, Hayes C, Kaminski MS. Acute megakaryocytic leukemia presenting as hypercalcemia with skeletal lytic lesions. *Eur J Hematol.* 2002;68:392–396.

[11] Malluche HH, Monier-Faugere MC. Risk of adynamic bone disease in dialyzed patients. *Kidney Int Suppl.* 1992;38: S62–S67.

[12] Johard U, Eklund A. Recurrent Lofgren's syndrome in three patients with sarcoidosis. *Sarcoidosis*. 1993;10(2):125–127.

[13] Iguchi H, Miyagi C, Kichinobu T, et al. Hypercalcemia caused by ectopic production of parathyroid hormone in a patient with papillary adenocarcinoma of the thyroid gland. *J Clin Endocrinol Metab*. 1998;83(8):2653–2657.

[14] Picolos MK, Sims CR, Mastrobattista JM, Carroll MA, Lavis VR. Milk-alkali syndrome in pregnancy. *Obstet Gynecol.* 2004;104(5 Pt 2):1201–1204.

[15] Hayden MR, Tyagi SC, Kolb L, Sowers JR, Khanna R. Vascular ossification-calcification in metabolic syndrome, type 2 diabetes mellitus, chronic kidney disease, and calciphylaxis-calcific uremic arteriolopathy: The emerging role of sodium thiosulfate. *Cardiovasc Diabetol*. 2005;4(1):4.

[16] Hebert SC. Extracellular calcium-sensing receptor: Implications for calcium and magnesium handling in the kidney. *Kidney Int.* 1996;50:2129–2139.

[17] Batuman V. Proximal tubular injury in myeloma. *Contrib Nephrol.* 2007;153:87–104.

[18] Brasier AR, Nussbaum SR. Hungry bone syndrome: Clinical and biochemical predictors of its occurrence after parathyroid surgery. *Am J Med.* 1988;84(4):654–660.