A rare case of acute kidney injury and anemia induced by hypercalcemia

Suparpit von Bormann,[1] Sirilak Suksompong,[2] Benno von Bormann[2]

[1]Institute of Nursing, Suranaree University of Technology, Nakhon Ratchasima; [2]Department of Anesthesiology, Siriraj Hospital, Bangkok, Thailand

Abstract

Hypercalcemia may result in acute kidney injury (AKI) and arterial hypertension. Anemia as a consequence of this constellation is nowhere described. A female patient underwent total thyroidectomy in 2007, since then being under continuous daily medication with 100 µg thyroxin, 1.6 g calcium and 1.0 µg alfacalcidol. In 2017, after accidentally overdosing alfacalcidol fourfold for several weeks leading to massive hypercalcemia (plasma calcium level 16.7 mg/dL), the otherwise healthy patient developed symptoms of AKI, such as serum creatinine 2.48 mg/dL, plus severe hypertension and acute anemia (hemoglobin concentration 10.2 g/dL). After cessation of calcium and alfacalcidol medication for 9 days, hypercalcemia and AKI symptoms and anemia recovered within 14 and after 62 days, respectively. The patient is currently free of complaints and has been sufficiently treated with half of the yearslong pre-event calcium/alfacalcidol dose. In conclusion, hypercalcemia with consecutive AKI after vitamin D overdose can occur asymptomatically. The treatment does not compulsorily include washout by hyperhydration and diuretics. AKI may lead to anemia, possibly caused by the deterioration of the release of erythropoietin.

Introduction

Hypercalcemia may lead to renal failure, for instance as a consequence of sarcoidosis, when granulomatous tissue produce Vitamin D in excess.[1] It may also result from renal resorption, retention (bones), or intestinal absorption.[2] Other important mechanisms include accidental overdosing or abusing of Vitamin D analogs.[3-5] In this regard, however, the development of acute anemia has not been reported yet in any of the published studies.

Case Report

A Thai female, aged 48 at the start of the event, had a normal body mass index (23.4 kg/m^2), good health, and no history of alcohol or smoking. The patient had no cardiovascular history, and the annual gynecological and internist checkups have been always insignificant. She had a normal to hypotensive blood pressure. She underwent total thyroidectomy in June 2007 for hyperthyroidism. Since then, she has been under continuous daily medication with thyroxin 100 µg, calcium carbonate 1.6 g, and alfacalcidol 1.0 µg.

After surgery, the patient started halfyearly checkups by internists and endocrinologists. Her clinical condition and laboratory status, including hemogram, were always normal. The level of serum calcium was always within the lowest normal range or slightly below. She was consistently normo-//hypotensive. She had an academic full-time job, and her physical fitness was normal.

In April 2017, the results of routine checkup showed normal values of blood pressure, serum creatinine, serum calcium, hemoglobin concentration, and thyroidal hormones. The level of Vitamin D was also normal (Table 1). Overall, there were no subjective complaints.

Day 0: September 4, 2017. Auxiliary finding during a routine blood pressure control at the dentist: massive hypertension 165/120 mmHg.

Day 1: consultation with a cardiologist. Cardiac function, including ECG, was normal, and the blood pressure still high with 160/125 mmHg; the laboratory test results revealed several pathologic findings, such as calcium serum level 16.7 mg/dL, serum creatinine 2.48 mg/dL (glomerular filtration rate: 24 mL/min), and hemoglobin concentration (cHb) 10.2 g/dL. Plasma parathyroid hormone was found to be low; and the level of vitamin D was normal. Urine status was normal with no dysuria, and stool had no occult blood. There was no bleeding, such as abnormal menstrual flow, and the patient had a usual diet. The patient did not report to suffer from any subjective symptoms.

Day 2: consultation with nephrologist and endocrinologist. The results of the nephrological inspection, including sonography, were unremarkable. The suspected diagnosis was consistent with acute kidney injury (AKI) caused by calcium intoxication. The therapy was continued by an endocrinologist.

Upon checking her schedule the same day, the patient noticed that at least four weeks before the event she accidentally took 4 alfacalcidol tablets of 1.0 µg instead of 4×0.25 µg, resulting in a daily dose of 4.0 instead of 1.0 µg.

Sole therapeutic measure is the complete cessation of calcium and alfacalcidol medication; hyperhydration and forced diuresis, as stated elsewhere,[1,6] were not applied. During this period, the patient was free of complaints, and there were no symptoms of hypocalcemia. On day 10, the patient re-started the calcium + alfacalcidol medication at a dose of 800 mg and 0.5 µg per day, respectively, which was half of the scheduled medication before the event. On that day blood pressure was already normal, level of creatinine decreasing but still elevated (1.65 mg/dL), and anemia persistent (cHb 10.1 g/dL).

On day 15, all parameters were normal, except cHb 10.3 g/dL.

Not until day 66 (November 9), cHb returned to normal 12.6 g/dL.

Ten months after the event, the patient was free of complaints, and the lab results were completely normal. However, the patient was still taking the calcium 800 mg and alfacalcidol 0.5 µg medication.

The work was performed at the Boromarajonani College of Nursing,

Correspondence: Benno von Bormann, Department of Anesthesiology, Siriraj Hospital, 2 Wanglang Road, Bangkok 10700, Thailand.
Tel.: 0066.0.24197990 – Fax: 0066.0.24113256.
E-mail: bvb@jodu.de

Key words: Anemia; Acute kidney injury; Drug overdose; Calcifediol.

Contributions: SvB conceived the idea for the article and managed the case; SS performed the literature review and assisted with the manuscript; BvB was the guarantor and wrote the article.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Received for publication: 14 Novemner 2018.
Revision received: 5 May 2019.
Accepted for publication: 27 May 2019.

Licensee PAGEPress, Italy
Clinics and Practice 2019; 9:1117
doi:10.4081/cp.2019.1117

Nonthaburi, Thailand; Patient's consent was obtained.

Discussion

We assume that a Vitamin D (alfacalcidol) intoxication with consecutive hypercalcemia caused the symptoms of AKI leading to hypertension, a constellation well known in patients with abuse or overdose of activated vitamin D.[7-9] Alfacalcidol (1-hydroxycholecalciferol) is an active Vitamin D3 metabolite, which does not require the second hydroxylation step in the kidney. We did not find any published cases or case series addressing exactly the problems and symptoms of the patient reported in this case study. Sharma *et al.*[10] reported a 61-year-old female patient with non-identical but similar symptoms, such as elevated calcium levels, anemia, and AKI. However, compared with our case, their patient had an elevated 1,25-dihydroxyvitamin level; she was finally diagnosed with sarcoidosis and successfully treated with glucocorticoids.

Remarkably, at no time – until the day of the event, during treatment, and afterward – did the patient suffer from subjective clinical symptoms indicating any kind of pathological process. Also, the level of plasma Vitamin D was never excessively elevated. No specific therapy, such as washout, was applied. Normalization of pathologic parameters proceeded smoothly and promptly after cessation of calcium and Vitamin D intake.

The observed anemia in our patient is nowhere described within the demonstrated constellation. The renal dysfunction may have caused deteriorated erythropoiesis leading to acute anemia;[11] this may be a large assumption, as we did not measure patients' plasma erythropoietin concentration. On the other hand, lacking alternative explanations for the acute anemia, this assumption cannot completely be denied. Apart from that, the interval between starting overdosing and the first appearance of symptoms was at least four weeks – long enough to affect the synthesis of kidney-produced erythropoietin.[12]

The problem-free halving of calcium and alfacalcidol intake compared to the yearslong medication is also difficult to explain. Even though the surgical report at that time described two intact parathyroid glands *in situ*, a residual function of the parathyroid gland after about 10 years is unlikely. Our case does not completely meet criteria for AKI,[13] because the interval without lab data between normal (April 2018) and pathological (September 2018) status is about 5 months. As a consequence, we do not know the patients' lab status immediately prior to her erroneous use of medication. As stated by Rahman *et al.*,[14] *Acute kidney injury is characterized by abrupt deterioration in kidney function, manifested by an increase in serum creatinine level with or without reduced urine output*. The criterion *abrupt* cannot be applied to the presented case.

Conclusions

Several patients after total thyroidectomy are dependent on calcium and Vitamin D analogs. Over- as well as under-dosing may have detrimental effects, whereby obvious clinical symptoms may be lacking. Meticulous clinical observation and laboratory monitoring, including measurement of serum calcium, creatinine, and hemogram, is mandatory. At the onset of symptoms of hypercalcemia-induced AKI, a complete cessation of the medication seems to be sufficient to control the complication.

Table 1. Blood pressure and laboratory data including normal values of a 47-year-old (the age at the beginning of the observation) female during 25-months period.

Date	BP mmHg	Calcium 8.6-10.0 mg/dL	Creatinine 0.51-0.95 mg/dL	cHb - female 12.0-14.9 g/dL	Vitamin D ≥20 ng/mL	PTH 15.0-65.0 ng/L	TSH 0.27-4.2 uIU/mL	FT4 0.93-1.70 ng/dL
Before the event								
July 2016	110/70	8.1		12.7	20.48	-	0.52	1.64
October 2016	105/65	7.8*		12.5	19.79	-	5.44*	1.25
April 2017	120/70	8.9	0.9	12.8	20.96	8.3*	2.08	1.36
Event								
Day 0 (September 4, 2017)	165/120*	Routine BP measurement at the dentist prior to teeth cleaning						
Day 1	160/125*	16.7*	2.48*	10.2*	23.8	7.27*	-	-
Cessation of calcium and alfacalcidol								
Day 4	145/105*	-	2.47*	-	-	-	-	-
Day 10	120/70	9.3	1.65*	10.1*	22.6	-	-	-
Re-start of calcium + alfacalcidol, half dose								
Day 15	110/65	9.3	1.21*	10.3*	-	-	2.32	1.74
Day 31	105/70	9.1	1.13*	11.4*	-	-	0.24	1.20
Day 66	100/65	9.4	0.87	12.6	16.75*	14.62	1.11	1.57
Actual checkup								
August 2018	95/70	8.9	0.91	13.4	-	16.22	1.28	1.34

BP, blood pressure; cHb, hemoglobin concentration; PTH, parathyroid hormone; TSH, thyroid stimulating hormone (IU, International units); FT4, free thyroxine. *Significant deviation from normal value.

References

1. Volpicelli G, Mussa A, Frascisco M. A case of severe hypercalcemia with acute renal failure in sarcoidosis: a diagnostic challenge for the emergency department. Eur J Emerg Med 2005;12:320-1.
2. Moyses-Neto M, Guimaraes FM, Ayoub FH, et al. Acute renal failure and hypercalcemia. Ren Fail 2006;28:153-9.
3. Boyd C, Moodambail A. Severe hypercalcaemia in a child secondary to use of alternative therapies. BMJ Case Rep 2016;2016.
4. Vyas AK, White NH. Case of hypercalcemia secondary to hypervitaminosis a in a 6-year-old boy with autism. Case Rep Endocrinol 2011;2011:424712.
5. Tebben PJ, Singh RJ, Kumar R. Vitamin D-mediated hypercalcemia: mechanisms, diagnosis, and treatment. Endocr Rev 2016;37:521-47.
6. Guerra V, Vieira Neto OM, Laurindo AF, et al. Hypercalcemia and renal function impairment associated with vitamin D toxicity: case report. J Bras Nefrol 2016;38:466-9.
7. Karpati RM, Mak RH, Lemley KV. Hypercalcemia, hypertension and acute renal insufficiency in an immobilized adolescent. Child Nephrol Urol 1991;11:215-9.
8. Wani M, Wani I, Banday K, Ashraf M. The other side of vitamin D therapy: a case series of acute kidney injury due to malpractice-related vitamin D intoxication. Clin Nephrol 2016;86:236-41.
9. Tollitt J, Solomon L. Hypercalcaemia and acute kidney injury following administration of vitamin D in granulomatous disease. BMJ Case Rep 2014;2014.
10. Sharma N, Tariq H, Uday K, et al. Hypercalcemia, anemia, and acute kidney injury: a rare presentation of sarcoidosis. Case Rep Med 2015;565243.
11. Zhang YJ, Li XM. [Relationship among the characteristics of anemia, serum level of erythropoietin and the renal tubulointerstitial injury in drug-associated renal parenchymal acute renal failure patients]. Beijing Da Xue Xue Bao Yi Xue Ban 2005;37:471-5.
12. von Bormann B, Weidler B, Schwanen N, et al. [Perioperative anemia and erythropoiesis]. Chirurg 1990;61:124-8.
13. Lieske JC, Chawla L, Kashani K, et al. Biomarkers for acute kidney injury: where are we today? Where should we go? Clin Chem 2014;60:294-300.
14. Rahman M, Shad F, Smith MC. Acute kidney injury: a guide to diagnosis and management. Am Fam Physician 2012;86:631-9.