Title: Severe acute hypocalcemia in a patient on hemodialysis

Authors: Christian Maalouly *[1], Benjamin Seront *[1], Johann Morelle[1,2], Michel Jadoul[1,2], Laura Labriola[1,2]

*CM and BS equally contributed to this work.

[1]Department of Nephrology, Cliniques Universitaires Saint-Luc, Brussels, Belgium.

[2]Institute of Experimental and Clinical Research, Université Catholique de Louvain, Brussels, Belgium.

Correspondence: Pr. Laura Labriola

Division of Nephrology

Cliniques Universitaires Saint-Luc

Avenue Hippocrate 10

B-1200 Brussels | Belgium

Tel. : +32 2 7641852 | Fax : +32 2 7642836

Email : laura.labriola@uclouvain.be

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THE CASE | SEVERE ACUTE HYPOCALCEMIA IN A PATIENT ON HEMODIALYSIS

A 56-year-old Caucasian man on maintenance hemodialysis for 5 years for end-stage kidney disease (ESKD) secondary to lithium-induced chronic interstitial nephropathy presented with acute and severe weakness of the 4 limbs.

His past medical history included bipolar disease, autoimmune thyroiditis and epilepsy. He had severe hyperparathyroidism with PTH levels above 2000 pg/mL for 4 years, despite the prescription of calcium-free phosphate binders and cinacalcet (Table 1). Poor adherence to this treatment was strongly suspected. Parathyroidectomy was repeatedly refused by the patient. Other current medications included valproate, olanzapine, cholecalciferol, epoetin alpha, and ferric carboxymaltose. He was dialyzed 4 hours three times a week (Kt/V 1.3). Potassium and calcium baths were 3 mmol/l and 1.5 mmol/l, respectively. The last dialysis session, performed 48 hours before admission, was uneventful.

Physical examination revealed hypotension (80/55 mmHg), bradycardia (45 bpm) and muscle weakness (2 of 5) of all 4 limbs. Predialysis blood tests showed acute, profound hypocalcemia (Table 1). Furthermore, a major drop of PTH level and an increase of total alkaline phosphatase level were noted (Table 1). Ionized calcium level, sampled two hours after the beginning of emergency dialysis, confirmed severe and persistent hypocalcemia (Table 1). Electrocardiogram showed bradycardia (50 bpm) with a long QT interval (517 milliseconds).

Severe hypocalcemia persisted (ionized calcium level 0.6 mmol/l) despite a 4-hour session of hemodiafiltration with a 1.5 mmol/l calcium dialysate and intravenous administration of 3 grams of calcium gluconate. The patient was transferred to the Intensive Care Unit.

What is your diagnosis?

THE DIAGNOSIS | PARATHYROID APOPLEXY FOLLOWING SPONTANEOUS BILATERAL PARATHYROID NECROSIS

The sudden and major drop of calcium and PTH levels suggested spontaneous necrosis of parathyroid adenoma(s), an entity known as parathyroid apoplexy.

Contrast-enhanced computed tomography (CT) of the neck documented two nodules with a low-density center and rim enhancement in the postero-inferior part of the thyroid, highly suggestive of bilateral parathyroid adenomas necrosis (Figure 1). PTH levels further decreased over the next days (Table 1), then started to increase and reached 1200 pg/ml after two weeks, and remained subsequently stable. The patient received high amounts of intravenous calcium gluconate for eight days. Daily hemodialysis with a dialysate calcium of 1.50 mmol/l was performed nine days in a row. Yet, total calcium level remained under the normal range for more than one month. Muscular strength returned to normal after several weeks.

Parathyroid gland spontaneous necrosis, also known as parathyroid apoplexy, is defined by infarction and/or hemorrhage within a parathyroid adenoma.[1-3] It is considered secondary to an imbalance between the growth of the adenoma and its blood supply, suggesting that large adenomas are more susceptible to ischemic insult.[1,3] Parathyroid apoplexy has mostly been documented in cases of spontaneous remission of primary hyperparathyroidism (PHPT) (around a hundred case reports).[1] In contrast, it has been reported very rarely in patients with secondary hyperparathyroidism (SHPT).[2,3] Clinical and biological presentation mimics the hungry bone disease that can be observed after surgical parathyroidectomy, with a sudden drop of PTH and calcium levels and a rise of alkaline phosphatase levels.[2,3] Most reported cases in case of PHPT and SHPT presented with acute symptoms of hypocalcemia. Rarely, hemorrhage may extend to

extracapsular space and cause symptoms ranging from local pain to airway compromise.[1] Although parathyroid apoplexy with hypocalcemia and spontaneous remission of hyperparathyroidism is a very rare phenomenon, less intense spontaneous necrosis may be more common and result only in asymptomatic moderate reduction of calcium and PTH levels.[1] Recurrence of hyperparathyroidism is usually observed after parathyroid apoplexy[3]. As parathyroid apoplexy is an uncommon complication, its management is not well established.[2,3] Urgent treatment of severe hypocalcemia is warranted: high dose calcium supplementation, daily hemodialysis with dialysate rich in calcium and high doses of calcitriol.

In conclusion, spontaneous parathyroid necrosis is very rare in SHPT. However, this condition should be included in the differential diagnosis of acute hypocalcemia with abrupt and unexplained drop in PTH levels in patients with severe hyperparathyroidism.

References

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Table 1. Laboratory findings.

	Normal range	Five days before	At presentation	Three days later
Total calcium (mmol/l)	2.15-2.5	**2.32**	**1.26**	**2.15**
Ionized calcium (mmol/l)	1.1-1.2	/	0.7	1.1
Phosphate (mmol/l)	0.8-1.45	1.04	1.29	0.8
Potassium (mmol/l)	3.5-5.5	5.6	5.77	4.7
Albumin (g/l)	35-52	42	44	/
Alkaline phosphatase (UI/l)	40-130	**556**	**709**	**832**
Bone alkaline phosphatase (µg/l)	4 –30	**/**	**/**	**> 120**
Intact PTH (pg/ml)	15-80	**2105**	**1231**	**686**
25-hydroxyvitamin D (ng/ml)	30-100	17	23	/

Legend to figure

Figure 1: Contrast-enhanced computed tomography scan of the neck showing the right parathyroid adenoma (13 x 12 mm) with low-density center and enhanced rim compatible with parathyroid necrosis (arrow).

Figure 1