Immobilization induced hypercalcemia

Edgar Alonso Cano-Torres[1]
Arnulfo González-Cantú[2]
Gabriela Hinojosa-Garza[3]
Fernando Castilleja-Leal[4]

[1] Internal Medicine resident, Escuela Nacional de Medicina Tecnológico de Monterrey, Messico
[2] Clinical Professor, Escuela Nacional de Medicina Tecnológico de Monterrey, Messico
[3] Undergraduate medical student, Escuela Nacional de Medicina Tecnológico de Monterrey, Messico
[4] Director of Internal Medicine Institute, Escuela Nacional de Medicina Tecnológico de Monterrey, Messico

Address for correspondence:
Edgar Alonso Cano-Torres
Internal Medicine resident
Escuela Nacional de Medicina Tecnológico de Monterrey
Messico
E-mail: ecano_t@hotmail.com

Summary

Immobilization hypercalcemia is an uncommon diagnosis associated with increased bone remodeling disorders and conditions associated with limited movement such as medullar lesions or vascular events. Diagnosis requires an extensive evaluation to rule out other causes of hypercalcemia.
This is a report of a woman with prolonged immobilization who presented with severe hypercalcemia. This case contributes to identification of severe hypercalcemia as a result of immobility and the description of bone metabolism during this state.

KEY WORDS: hypercalcemia; immobilization.

Background

Albright described immobilization-associated hypercalcemia in 1941 (1). Despite the fact that insufficient evidence has been published in specialized journals, it has been described as a complication in patients with prolonged prostration ever since; especially in young adults with immobilization, such as those with spinal cord injuries (2, 3).

Case report

A 35-year-old woman with no significant past medical history suffered a severe traumatic brain injury related to a cycling accident. Following the initial treatment of her CNS injury, she remained in a chronic immobilization state and after eight months in intensive care unit she presented with hypercalcemia.
Elevated ionized and total calcium levels were associated with diminished PTHi levels and increased calcium excretion. 25-hidroxy vitamin D and 1,25-dihydroxyvitamin D levels did not justify the presence of hypercalcemia and elevated N-telopeptides (Table 1). Thyroid and adrenal gland function were found normal. Due to the absence of past medical history and the acute onset of hypercalcemia, among the differential diagnosis only primary hyperparathyrodism, vitamin D induced hypercalcemia, and immobilization hypercalcemia were considered (Figure 1).
Rehabilitation therapy was initiated and fluid input was increased along with diuretic addition with no considerable improvement. For this reason, an infusion of 4 mg zoledronic acid was added to her treatment. Two months after serum calcium normalization the patient persists with her supportive therapy and absence of hypercalcemia relapse.

Table 1 - Patient biochemical parameters. LDH: lactic dehydrogenase.

Parameter	Result	Units	Reference value
Creatinine	1.1	mg/dl	(.6-1.1)
Albumin	2.8	gr/dl	(3.5-5.0)
Alkaline Phosphatase	133	U/L	(40-150)
LDH	170	U/L	(125-243)
Phosphorus	3.2	mg/dl	(2.3-4.7)
Total Calcium	16.3	mg/dl	(8.4-10.2)
Corrected Calcium	17.26	mg/dl	(8.4-10.2)
Ionized Calcium	2.29	mmol/L	(1.0-1.2)
24 h Urinary Calcium	400	mg	(100-300)
Intact Paratohormone	14.3	pg/ml	(15.0-68.3)
25-hidroxi Vitamin D	26.7	ng/ml	(> 30)
1,25-dihidroxi Vitamin D	5.8	pg/ml	(10-75)
Bone alkaline phosphatase	17.8	Ug/L	(0-21.3)
N-telopeptide	400	nmol BCE/L	(6.2-19)

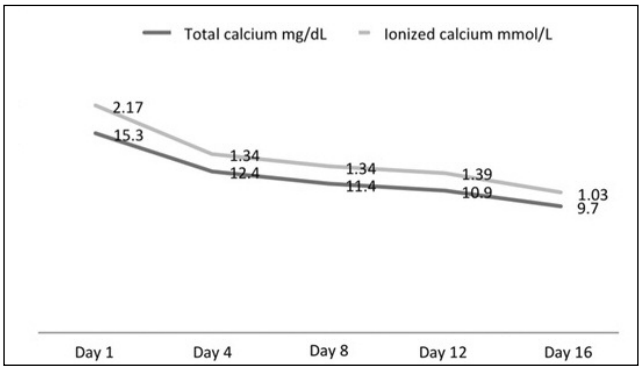

Figure 1 - Sequential ionized and serum calcium changes at the beginning of treatment with zoledronic acid.

Discussion

Immobilization hypercalcemia is an uncommon diagnosis predominately present in children or young adults with limited mobility during the first four to six weeks after the precipitating injury/immobilization; nevertheless it can present even months after (4).

Immobilization hypercalcemia diagnosis requires an exhaustive evaluation to rule out more likely hypercalcemia causes. First, a relationship between hypercalcemia with PTHi and vitamin D serum levels is established (5, 6). Cancer associated hypercalcemia should be excluded, if guided by clinical suspicion. The presence of elevated NTX levels and low to normal bone-specific alkaline phosphatase validate calcium bone loss. The negative balance in bone formation is due to the increased sclerostin secretion by osteocytes, which diminishes the bone formation stimuli by blocking the Wnt-Runx2 pathway in the osteoblast (7, 8).

Hypercalcemia immobilization is a diagnosis that has to be accounted for in patients with immobilization and hypercalcemia. Calcium levels greater than 13 mg/dl do not rule out immobilization as the cause of hypercalcemia. Early treatment has to be focused on hydration and loop diuretics; in no improvement is detected, zoledronic acid is indicated (9).

Conclusion

The most used treatment for immobilization hypercalcemia is zoledronic acid infusion, with a gradual bone metabolism reduction. Normocalcemia is reached generally during the fifth day. Denosumab, an authorized antiresorptive drug for the treatment of osteoporosis has been used more frequently but its use is associated with potential side effects and there is a lack of evidence to recommend its use on a routine basis (10).

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