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Case Report

Normal alkaline phosphatase level in a patient with primary hyperparathyroidism due to parathyroid adenoma

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Abstract

Primary hyperparathyroidism is relatively an uncommon condition, where the majority of cases present asymptomatically after biochemical testing showing a mild hypercalcemia and elevated parathyroid hormone (PTH) level. Long-standing elevated serum calcium level can lead to renal insufficiency. High serum PTH levels are associated with elevated alkaline phosphatase (ALP) levels in the general population. We present, an 89-year-old woman who initially manifested acute renal failure due to hypercalcemia and, finally, was diagnosed parathyroid adenoma. An interesting issue that drew our attention was the elevation of serum PTH level, despite the normal serum ALP concentration. It is the most important topic in this presentation. According to direct relationship between serums intact PTH and ALP in primary hyperparathyroidism, any failure in increasing levels of ALP, draw our attention to a range of diseases. Differential diagnoses for low ALP activity are mentioned in this case report.

Keywords: Primary hyperparathyroidism, Parathyroid hormone, Alkaline phosphatase

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Introduction

Primary hyperparathyroidism as a condition with a high bone turnover is caused by an increased secretion of parathyroid hormone (PTH). It is usually originated from a solitary parathyroid adenoma. PTH through its complex actions on the kidneys, gastrointestinal tract, and the bones is involved in the hemostasis of vitamin D, calcium, and phosphate (1). Primary hyperparathyroidism occurs with no symptoms in up to 80% of patients and increased levels of PTH are characterized during work up of hypercalcemia (2). Long-standing elevated serum calcium level can lead to renal insufficiency which is dependent to duration and degree of hypercalcemia. Generally hyperparathyroidism is diagnosed through parathyroid immunoassay. When high PTH has been confirmed, the high serum level of calcium is confirmatory factor for primary hyperparathyroidism. Other biochemical agents are measured here in these cases such as: serum alkaline phosphatase (ALP) which is often elevated, serum chloride/phosphate ratio (33 or more in most patients), serum phosphate, urinary cAMP and intact PTH (iPTH) levels that are elevated too. Decrease in serum level of this enzyme is less considered than its increase. Here we describe a patient with elevated serum PTH level due to primary hyperparathyroidism who had a low serum ALP and discuss about the causes can lead to these clinical conditions. Some other interesting features of this case such as acute renal failure (ARF) due to primary hyperparathyroidism are also discussed. To our knowledge this is the first such reported case in Iran.

Case Presentation

An 89-year-old woman was referred to our emergency department in November 2013 because of hypercalcemia and recently developed acute impairment of renal function. Symptoms included anorexia, constipation, weakness, fatigue, dyspepsia, frequency, and urinary incontinence. The patient had been well until two months before admission, when she had fever, chills, and right flank pain. The laboratory findings at that time are given in Table 1.

She reported a history of weight loss of 3 kg within the

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Implication for health policy/practice/research/ medical education

Clinical manifestation of primary hyperparathyroidism has shifted from a symptomatic disease to no specific symptoms ("asymptomatic" primary hyperparathyroidism). However, the most common cause of hypercalcemia is primary hyperparathyroidism and it should be considered in the patients with an elevated serum calcium level.

past 3 months. She was diagnosed with hypertension about two years ago and her blood pressure was under controlled by anti-hypertensive drugs. Patient was not on calcium or vitamin D supplements. There was no personal or family history of hypercalcemia. She had no history of diabetes mellitus, hypothyroidism, and other diseases. On admission, she had a pulse rate of 80 bpm, blood pressure of 130/80 mmHg, respiratory rate of 12 breath/minute and temperature of 37 °C and the physical examination was unremarkable. Initial laboratory tests showed hypercalcemia, elevated serum creatinine, and normal value of ALP. Laboratory findings at presentation are shown in Table 2. The radiography of the chest were also unremarkable.

In the emergency department, she was given intravenous normal saline, furosemide, and empirical antibiotics. After several days of treatment, her serum creatinine level decreased from 1.9 mg/dl to 1.1 mg/dl and serum calcium concentration reduced from 14.0 mg/dl to 11.1 mg/dL. A renal ultrasound showed normal findings. She had a recent normal mammogram and no evidence of malignancy on ultrasonography of abdomen/pelvis. Bone scan was negative for bone metastasis. In further workup, the sestamibi scan showed a right parathyroid adenoma, which was confirmed by pathology result (Figure 1). Primary hyperparathyroidism diagnosis was suggested by elevated serum calcium, markedly increased level of PTH, and parathyroid adenoma. Surgical exploration of the neck revealed three normal parathyroid glands and one right parathyroid mass. Two days after operation, the PTH level was normal. Final pathology permanent sections were interpreted as parathyroid adenoma. Repeat assessment 2 weeks later showed resolution of hypercalcemia with calcium of 10.3 mg/dl.

Table 1. Laboratory data two months prior to her admission

Laboratory parameters	Value	Laboratory parameters	Value
BUN (mg/dl)	31	Serum sodium (mEq/l)	138
Serum creatinine (mg/dl)	1.4	Serum potassium (mEq/l)	4
FBS (mg/dl)	95	AST (U/l)	22
Triglyceride (mg/dl)	252	ALT (IU/l)	25
Cholesterol (mg/dl)	219	Urinalysis	Normal

BUN, Blood urea nitrogen; FBS, Fasting blood sugar; AST, Aspartate aminotransferases; ALT, Alanine aminotransferase

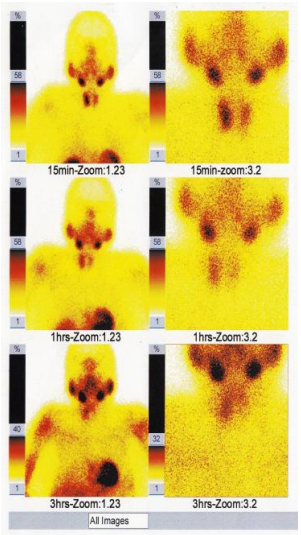

Figure 1. Sestamibi parathyroid glands scan shows an adenoma in the lower portion of thyroid lobe

Table 2. Laboratory data at presentation

Laboratory parameters	Patient	Normal range	Laboratory parameters	Patient	Normal range
BUN (mg/dl)	43	7.9–20	Serum sodium (mEq/l)	139	135–145
Serum creatinine (mg/dl)	1.9	0.6–1.4	Serum potassium (mEq/l)	4.8	3.5–5.5
Serum albumin (g/dl)	3.9	3.5–5	Hemoglobin (g/dl)	13	12.3–15.3
Alkaline phosphatase (U/l)	221	Up to 240	Urinalysis	Normal	-
Serum calcium (mg/dl)	14	8.6–10.2	Serum Uric acid (mg/dl)	9.2	3.5–7.3
ESR 1st hour (mm/hour)	12	Up to 30	Serum 25-OH vitamin D (ng/ml)	20.4	10–65
iPTH (pg/ml)	239	6–40	TSH (MicIu/ml)	7.2	0.4–4.2
T3 (ng/ml)	0.8	0.5–2.2	T4 (mcg/dl)	72	45–126
Urine Bence- Jones protein test	Negative	Negative	Anti-TPO antibody (IU/Ml)	287	0–75
Serum phosphorus(mg/dl)	2.6	2.5–4.5	Serum magnesium(mg/dl)	1.6	1.7–2.4

BUN, Blood urea nitrogen; iPTH, intact parathyroid hormone;

Discussion

Primary hyperparathyroidism is relatively an uncommon condition, where the majority of cases present asymptomatically after biochemical testing showing a mild hypercalcemia and elevated PTH level (1-3). Causes of hypercalcemia encompasses a wide range which include abnormal parathyroid gland function, malignancy, vitamin D metabolic disorders, disorders related to high bone-turnover rates and renal failure. Hypercalcemia associated with renal failure occurs in different clinical situation such as: hypercalcemia in hemodialysis patients, after renal transplantation, in chronic renal failure (CRF) patients without complications and in acute renal failure (ARF) due to rhabdomyolysis at the phase of diuresis and renal manifestations. ARF, CRF, nephrolithiasis, and decreased urinary concentrating ability are the most common renal manifestations of hypercalcemia (2-6). In this paper we reported a case referred to hospital because of elevated serum creatinine and hypercalcemia. An interesting issue that drew our attention was the elevation of serum PTH level, despite the normal serum ALP concentration. It is the most important topic in this presentation. She did not have history of vitamin D deficiency. The direct relationship between serum iPTH and ALP in primary hyperparathyroidism has been reported in previous studies (3). ALP is an enzyme that is secreted from five different organs included intestine, placenta, kidney, liver, and bone (4-7). Bone ALP is secreted by osteoblast cells. It is involved in the bone formation and skeletal mineralization. PTH stimulates osteoblast activity and thus increases level of ALP in blood (8,9). New Studies suggest that serum ALP level is a predictor for post-operative hypocalcaemia (POH). It can complicate after parathyroid adenectomy. Loke *et al.* in their study found that "patients with a pre-operative ALP less than 340 U/l are unlikely to have symptomatic POH" after parathyroid adenectomy (10). It is of interest that we introduce a patient who initially manifested acute renal failure due parathyroid adenoma and serum AlP level was not elevated. Clinical conditions associated with low ALP activity is summarized in Table 3 (11).

According to the laboratory data of the presented case, she had low magnesium concentration and hypothyroidism. On the other hand, zinc and magnesium are necessary for ALP activity in serum (12). The association between low ALP and zinc concentrations has been described in patients receiving total parenteral nutrition (13). Also, decreased serum ALP activity has been described in patients with hypomagnesaemia (14). So the normal serum ALP levels in our patient may be related to decrease in serum magnesium concentration. Also previous studies have shown the association between low serum ALP activity and hypothyroidism that was reversed after successful treatment of hypothyroidism (15). It is reported that thyroid hormones and vitamin B12 are necessary for activity of osteoblast cells and production of ALP by them (16). So in some cases the low level of serum ALP can be related to the hypothyroidism. Furthermore, the low serum concentrations of zinc and magnesium cations in hypothyroidism may also lead to the decreased serum ALP activity. It is said that restoring these cations to their normal level, can also put ALP in normal rang (16,17). Hypothyroidism in our patient may be lead to not increasing serum ALP concentration in condition with hyperparathyroidism. According to medical history and other laboratory finding of this case, she did not have other clinical situation associated with low ALP activity that mentioned in Table 3.

Conclusion

Clinical manifestation of primary hyperparathyroidism has shifted from a symptomatic disease to no specific symptoms ("asymptomatic" primary hyperparathyroidism). However, the most common cause of hypercalcemia is primary hyperparathyroidism and it should be considered in the patients with an elevated serum calcium level. It is necessary to pay attention to PTH level and ALP concentration during work up of hypercalcemia. According to direct relationship between serum iPTH and ALP in primary hyperparathyroidism, any failure to increasing levels of ALP, draw our attention to a range of diseases. Differential diagnoses for low ALP

Table 3. Clinical conditions associated with low ALP activity

Zinc deficiency	Pernicious anemia
Magnesium deficiency	Protein/calorie deficiency
Hypophosphatemia	Estrogen replacement therapy in postmenopausal women
Cardiac surgery and cardiopulmonary bypass	End-stage osteopenia of chronic renal osteodystrophy
Artifacts associated with collection of blood in EDTA or oxalate anticoagulant	Achondroplasia and cretinism in children
Hypothyroidism	Vitamin C deficiency
Severe anemia	Milk-alkali syndrome, excess ingestion of vitamin D, inanition, celiac disease, hypoparathyroidism, intake of radioactive heavy metal, drugs such as clofibrate, recent massive blood transfusions, or post hepatic resection and transplantation

activity were mentioned in this literature review.

Authors' contributions

All authors wrote the paper equally.

Conflict of interests

None of the contributing authors has any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

Ethical considerations

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