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Case report

HYPERTENSION IN PRIMARY HYPERPARATHYROIDISM: A CASE REPORT OF ECTOPIC PARATHYROID ADENOMA

ХИПЕРТЕНЗИЈА ПРИ ПРИМАРЕН ХИПЕРПАРАТИРЕОИДИЗАМ: СЛУЧАЈ НА ЕКТОПИЧНА ПАРАТИРЕОИДНА АДЕНОМА

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Abstract

Primary hyperparathyroidism is a condition characterized by excessive production of parathyroid hormone, often caused by an adenoma or hyperplasia of the parathyroid gland. One of the rare presentations of primary hyperparathyroidism is the development of an ectopic parathyroid adenoma, which can be challenging to diagnose and localize. Hypertension is observed seen in many cases of primary hyperparathyroidism (PHPT), although the exact mechanism is yet unclear. This paper aims to provide a comprehensive review of the current understanding of primary hyperparathyroidism, with a focus on the presentation of ectopic adenomas and the relationship between primary hyperparathyroidism and resistant hypertension. While most parathyroid adenomas are located in the normal anatomical position of the parathyroid glands, a small percentage (approximately 2-5%) can occur in ectopic locations, such as the thyroid gland, carotid sheath, or mediastinum. The atypical location of ectopic parathyroid adenomas can make them more difficult to identify and remove surgically, which can be difficult diagnostic challenge. The prevalence of primary hyperparathyroidism has been estimated to be around 0.1-0.4% in the general population, with a higher incidence in postmenopausal women.

The imaging tests consist mainly of an initial 99mTc-sestamibi SPECT/CT. Sensitivity and specificity of sestamibi scans are between 73%-80%, respectively. Clinical sensitivity is increased to 96% when sestamibi scans are combined with ultrasound.

Keywords: hypercalcemia, hyperparathyroidism, hypertension, ectopic parathyroid adenoma

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Абстракт

Примарниот хиперпаратироидизам е состојба која се карактеризира со прекумерно производство на паратироиден хормон, често асоцирано со аденом или хиперплазија на паратироидната жлезда. Една од ретките манифестации на примарен хиперпаратироидизам е ектопичен аденом на паратироидната жлезда, кој може да биде предизвик да се дијагностицира и локализира. Хипертензија е забележана во многу случаи на примарен хиперпаратироидизам (PHPT), иако точниот механизам сè уште е нејасен. Овој труд има за цел да обезбеди сеопфатен преглед на примарниот хиперпаратироидизам, со фокус на презентацијата на ектопични аденоми и корелацијата помеѓу примарниот хиперпаратироидизам и резистентната хипертензија. Повеќето паратироидни аденоми анатомски локализирани на параторироидната жлезда,мал процент (2-5%) се локализирано на тироидната жлезда, каротидната обвивка или медијастинумот. Атипичната локација на ектопичните паратироидни аденоми може да го отежне нивното идентификување и отстранување хируршки, што може да биде тежок дијагностички предизвик. Преваленцата на примарен хиперпаратироидизам е проценета на околу 0,1-0,4% кај општата популација, со повисока инциденца кај жените во постменопауза. Визуелизирачки метод за дијагноза на паратироидните аденоми е 99mTc-sestamibi SPECT/CT. Сензитивноста и специфичноста на скенирањата со 99mTc-sestamibi SPECT/CT. се помеѓу 73%-80%, соодветно. Клиничката сензитивност се зголемува на 96% кога 99mTc-sestamibi SPECT/CT се комбинира со ултрасонографски преглед.

Клучни зборови: хиперкалцемија, хиперпаратироидизам, хипертензија, ектопичен паратироиден аденом

Introduction

Primary hyperparathyroidism leads to increased levels of parathyroid hormone (PTH), which can alter calcium metabolism. Elevated calcium levels are associated with an increased risk of cardiovascular diseases by promotion of calcification and impairment of endothelial cell function. Hypertension is a common comorbidity associated with primary hyperparathyroidism, with studies suggesting that 40% of patients with primary hyperparathyroidism have hypertension [1]. Effective management of PHPT requires a multidisciplinary approach that includes comprehensive treatment of both hypertension and hypercalcemia, and surgical removal of parathyroid adenoma. Recognizing this association is vital for timely diagnosis and management, which may help to mitigate cardiovascular complications in patients with PHPT [2]. While parathyroidectomy remains to be primary treatment, it is important not to overlook the role of medications, such as bisphosphonates, cinacalcet and vitamin D, during the preoperative period [3].

Case Report

A 55-year-old female presented to the University Clinic for Cardiology with a hypertensive crisis; the blood pressure was measured at 250/160 mmHg, and the patient had a poor response to antihypertensive medications. She underwent echocardiography and carotid artery ultrasonography, both of which were unremarkable. Then, the patient was referred to the University Clinic for Nephrology. Renal ultrasound depicted a calculus in the right kidney. Blood test results revealed increased total and ionized calcium levels, as well as a low phosphate level along with increased PTH levels, findings consistent with a diagnosis of PHPT. Therefore, the patient was referred to our clinic.

Table 1. Initial laboratory results of the patient

Laboratory findings	Patient's results	Reference range
Inorganic phosphate	0.62	0.8 – 1.4 mmol/L
Calcium	3.2	2.1 -2.6 mmol/L
Ionized calcium	1.85	1.12 -1.31 mmol/L
PTH	301	10-69 pg/ml

A thyroid ultrasound revealed no significant findings. An ECG indicated left ventricular hypertrophy. DEXA scan confirmed high-grade osteoporosis in the spine and in the femur neck on both sides. The patient's antihypertensive regimen included calcium channel blockers (nifedipine 40 mg), angiotensin II receptor antagonists (valsartan 320 mg), mineralocorticoid receptor antagonists (spironolactone 25mg), and a loop diuretic (furosemide 40 mg).

In order to alleviate hypercalcemia, we administered 4 mg of zoledronic acid intravenously. Consequently, the ionized calcium level returned to normal, and PTH levels increased further. Following that, blood pressure control occurred. However, the duration of the effect was short, and severe hypertension ensued several days later when hypercalcemia reappeared.

Table 2. Laboratory results after administration of zoledronic acid

Laboratory findings	Patient's results	Reference range
Inorganic phosphate	0.35	0.8 – 1.4 mmol/L
Calcium	2.56	2.1 -2.6 mmol/L
Ionized calcium	1.28	1.12 -1.31 mmol/L
PTH	1034	10-69 pg/ml

A parathyroid scan using 99mTc-MIBI with SPECT/CT revealed hyperfunctional parathyroid tissue ectopically located in the retrosternal region. While waiting for surgical treatment, cinacalcet was initiated, with favorable outcomes in reducing calcium levels and controlling blood pressure.

Table 3. Laboratory results under treatment with cinacalcet

Laboratory findings	Patient's results	Reference range
Ionized calcium	1.38	1.12 -1.31 mmol/L
PTH	454	10-69 pg/ml

Discussion

Due to high blood pressure, worsened by hypercalcemia, the patient was treated with four antihypertensive medications, such as calcium channel blockers (nifedipine 40 mg), angiotensin II receptor blockers (valsartan 320 mg), a mineralocorticoid receptor antagonist (spironolactone 25 mg), and a loop diuretic (furosemide 40 mg). Intravenous zoledronic acid is the choice of treatment for severe hypercalcemia. However, as seen in our case, under extreme circumstances, its effects may be temporary. Consequently, therapy with cinacalcet 60 mg twice daily was initiated, resulting in significant improvement in calcium levels and patient's blood pressure control as well.

We also provided vitamin D supplementation. Vitamin D supplementation is important in terms of preventing postoperative hypocalcemia in the setting of "hungry bone disease". The patient underwent a CT scan of the neck and chest to determine the precise location of the parathyroid adenoma. Subsequently, the adenoma was excised via transsternal thoracotomy. Pathohistological analysis indicated the presence of oxyphilic adenomas. Following surgery, the patient was treated with 1500 mg of calcium carbonate and 2000 IE of vitamin D, and the patient's calcium and PTH levels returned to the reference range. Primary hyperparathyroidism is a

challenging diagnosis given that one of the symptoms, hypertension, is often treated at primary care and many neglect ordering further tests to investigate the true cause. With the given symptoms and laboratory results, an ectopic adenoma takes time to diagnose given the unusual location and the limited resources available in small countries. Conservative treatment may ease symptoms and make little improvements in the patient's daily life, but ultimately surgery is the mainstay treatment along with lifelong supplementation.

Conclusion

Based on the patient's history and laboratory investigations, elevated total and ionized calcium, and abnormally high levels of PTH, accompanied by low inorganic phosphates, a diagnosis of PHPT was made. Further investigations with SPECT/CT revealed an ectopically located parathyroid adenoma in the mediastinum. Primary hyperparathyroidism is a condition characterized by the overproduction of PTH, mostly due to a parathyroid, adenoma although it may also arise from ectopic parathyroid adenoma [9]. The prevalence of asymptomatic hypercalcemic patients is significant [8]. Treatment of hypertension in the setting of PHPT can be quite challenging and complicated in cases of ectopic parathyroid adenoma. Bisphosphonates are an effective treatment for hypercalcemia; however, their efficacy may be temporary in cases of severe PHPT. The combination of bisphosphonates, cinacalcet, has proven to be an effective treatment for hypercalcemia [4-7]. We recommend a level of consideration for hypercalcemia to be maintained in patients presenting with refractory hypertension or hypertensive crises. Treatment should not be overlooked but surgery should not be delayed if the improvements we want are not achieved.

Conflict of interests: None declared.

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