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RENAL CALCIFICATIONS IN SYMPTOMATIC PRIMARY HYPERPARATHYROIDISM WITH MASSIVE HYPERCALCEMIA IN 47-YEAR-OLD-MAN: A CASE REPORT WITH LITERATURE REVIEW

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Abstract

Primary hyperparathyroidism (PHPT) is a disorder of the parathyroid glands where there is excessive production of PTH from one or more parathyroid glands. Eventually, it causes an increase in calcium levels in the blood or hypercalcemia. We report the case of a 47-year-old man with major complaints of right waist pain. Pain is felt up to the thigh and worsens when walking or doing an activity. On local examination of the neck area, there was no visible mass the inspection, and on palpation, there was no lump or mass in the neck area. There was tenderness in the right and left costovertebral angle (CVA) on abdominal examination. On laboratory examination, PTH levels were 455.8 pg/Ml. Calcium levels were 13.5 mg/dL, creatinine was 2.6 mg/dL, urea was 64.9 mg/dL. On abdominal ultrasound, multiple hyperechoic lesions were found on the right and left kidneys measuring 6 – 12 mm with the impression of nephrolithiasis and on urological CT scan without contrast, multiple calcifications in both kidneys were found. The patient underwent percutaneous nephrolithotomy (PCNL) to remove kidney stones.
Keywords: Primary hyperparathyroidism (PHPT), Massive Hypercalcemia, Case Report

Abstrak

Hiperparatiroidisme primer (PHPT) adalah kelainan kelenjar paratiroid di mana terjadi produksi PTH yang berlebihan dari satu atau lebih kelenjar paratiroid. Akhirnya, itu menyebabkan peningkatan kadar kalsium dalam darah atau hiperkalsemia. Kami melaporkan kasus seorang laki-laki berusia 47 tahun dengan keluhan utama nyeri pinggang kanan. Nyeri dirasakan hingga ke paha dan diperparah saat

berjalan atau melakukan aktivitas. Pada pemeriksaan lokal daerah leher tidak terlihat adanya massa pada pemeriksaan, dan pada palpasi tidak ada benjolan atau massa pada daerah leher. Terdapat nyeri tekan pada costovertebral angle (CVA) kanan dan kiri pada pemeriksaan abdomen. Pada pemeriksaan laboratorium didapatkan kadar PTH 455,8 pg/Ml. Kadar kalsium 13,5 mg/dL, kreatinin 2,6 mg/dL, ureum 64,9 mg/dL. Pada USG abdomen ditemukan lesi hiperekoik multipel pada ginjal kanan dan kiri berukuran 6 – 12 mm dengan kesan nefrolitiasis dan pada CT scan urologis tanpa kontras ditemukan kalsifikasi multipel pada kedua ginjal. Pasien menjalani nephrolithotomy perkutan (PCNL) untuk menghilangkan batu ginjal.
Kata Kunci: Primary hyperparathyroidism (PHPT), Massive Hypercalcemia, Case Report

INTRODUCTION

PHPT is a disorder of the parathyroid glands in which there is excessive secretion of PTH from one or more parathyroid glands. It ultimately causes an increase in blood calcium levels or hypercalcemia.[1]

In most cases, a parathyroid adenoma can cause primary hyperthyroidism, MEN (multiple endocrine neoplasias) types 1 and 2, hyperparathyroidism-jaw tumour syndrome, and familial hyperparathyroidism. In rare cases, it can be caused by parathyroid carcinoma.

We report a case of primary hyperparathyroidism with a suspected hyper parathyroid adenoma with a PTH level of 455.8 pg/mL and a blood calcium level of 13.5 mg/dL.

CASE REPORT

A 47-year-old man came to the Endocrine, Metabolism and Diabetes clinic at RSUD K.R.M.T Wongsonegoro on May 17, 2022 with complaints of pain in the right waist. The pain radiates to the thigh and worsens when walking or doing an activity. When walking, the patient feels weak and pain in both knees. The patient's pain has been felt since 2 years ago and has worsened in the last 3 months. The patient is also often get tired since last month and feels loss of appetite. The patient was not obese, had no history of abdominal and legs trauma, and did not experience pain when urinating. The patient denied pain in the epigastric area, nausea, vomiting, and fever. The patient had a history of hypertension but was controlled with daily anti-hypertensive drugs.

On physical examination, the patient was found to be weak, compost mentis, GCS 15 (E4M6V5), blood pressure 152/95 mmHg, pulse 90 x/minute, temperature 37°C, respiratory rate 20x/minute, SpO2 99%. Local examination in the neck area, when the inspection was carried out there was no visible mass, and on palpation there was no lump or mass in the neck area. On abdominal examination, tenderness was found at the costovertebral angle (CVA) dextra and sinistra.

On laboratory examination, PTH levels were 455.8 pg/mL, ferritin 288.8 ng/mL, UIBC 191 ug/dL, serum Fe 75.0 ug/dL, calcium levels 13.5 mg/dL, potassium 2.80 mmol. /L, sodium 138.0 mmol/L, creatinine 2.6 mg/dL, and urea 64.9 mg/dL.

On ultrasound examination, parenchymal echogenicity appeared to be increased and multiple hyperechoic lesions appeared on the right and left kidneys measuring 6-12 mm in size and simple cysts on the left kidney with a size of 14 mm.

On CT-scan urology without, on the left and right kidneys, multiple calcifications were seen in both parenchyma.

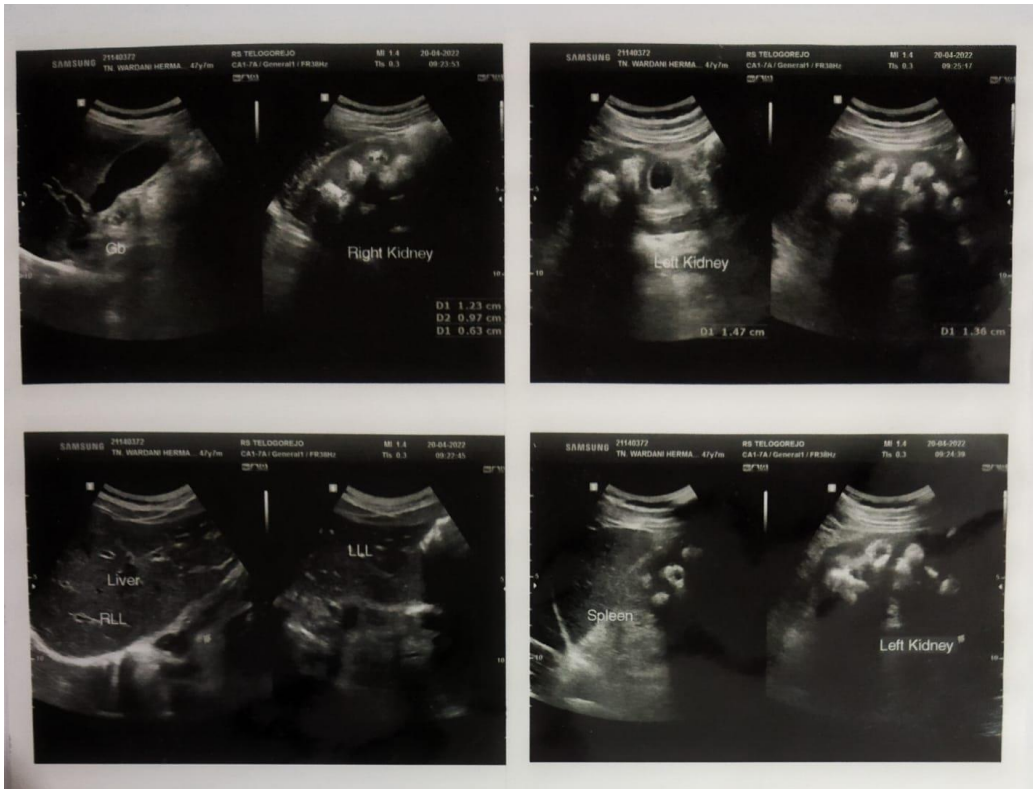

Figure 1: On abdominal ultrasound, multiple hyperechoic lesions were found on the right and left kidneys measuring 6 – 12 mm with the impression of nephrolithiasis with a differential diagnosis of nephrocalcification. There was also an increase in echogenicity in both kidneys with diffuse parenchymal changes in both Brenbridge 2 kidneys.

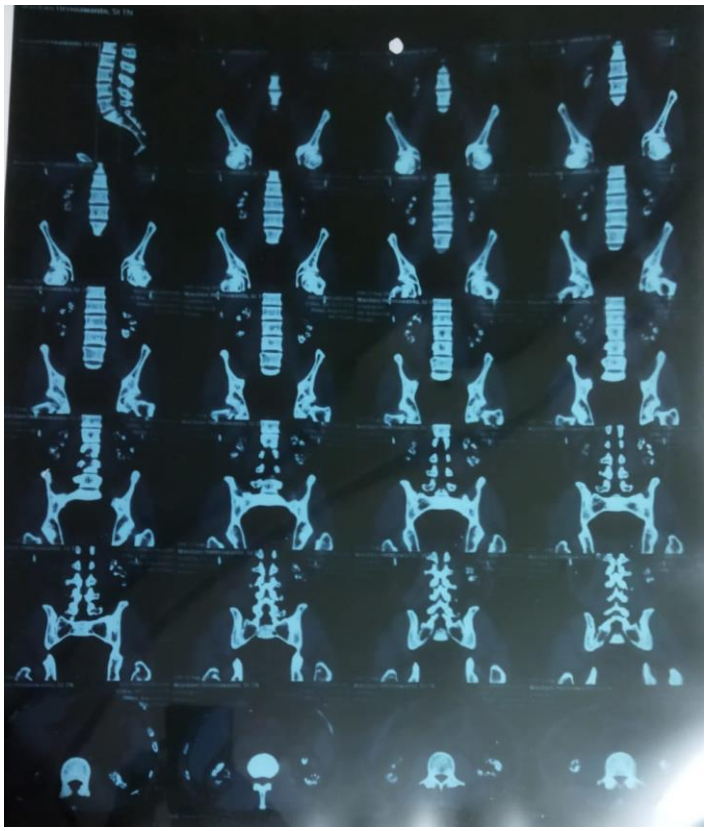

Figure 2: On CT-scan urology without contrast, multiple calcifications were found in both kidneys with a differential diagnosis of nephrocalcinosis and multiple cysts in the left kidney.

The patient have hyperparathyroidism that cause hypercalciuria on the blood, the excess of calcium in the blood have cause the stone in the renal to form, therefore the patient on CT scan without contrast there is multiple calcification in both kidneys, that lead the physician to do Parathyroidectomy to reduce the parathyroid production on the body which will reduce the complication of hyperparathyroid in this patient.

RESEARCH METHODS

The research method used in this study is library research. This study aims to gain an in-depth understanding of the topic being researched by utilizing available sources of information in the form of relevant documents, journals, books, reports and articles. The data collection instrument used in this research is documentation. Documentation involves collecting data from various sources in written or recorded form.

Researchers carry out the process of selecting and evaluating the documents that have been found. Documents that are considered relevant, valid and of good quality are used as the main data source in the research. Next, the researcher reads, analyzes, and synthesizes the contents of these documents. Important information found in these documents is then used to build arguments or conclusions in research.

RESULT AND DISCUSSION

PHPT is a disorder of the parathyroid glands in which there is excessive secretion of PTH from one or more parathyroid glands and ultimately causes an increase in blood calcium levels or hypercalcemia.[1]

Primary hyperparathyroidism is a relatively common endocrine disorder, with an estimated prevalence of one to seven cases per 1000 adults. The global incidence varies widely from 0.4 to 21.6 cases per 100,000 people per year. The prevalence of PHPT increased with a predilection of 53.8% in women and 46.2% in men during the study period conducted by Yeh MW et al.[2] Currently, there are insufficient data on the epidemiology of hyperparathyroidism in Indonesia.

Parathyroid-dependent hypercalcemia can be caused by parathyroid adenoma in most cases, MEN (multiple endocrine neoplasia) types 1 and 2, hyperparathyroidism-jaw tumor syndrome, and familial hyperparathyroidism. In rare cases, it can be caused by parathyroid carcinoma, calcium-sensing receptor mutations, and side effects of treatment with lithium. Meanwhile, parathyroid-independent hypercalcemia can be caused by malignancy, granulomatous diseases, hyperthyroidism, therapy with thiazides, vitamin D intoxication, milk-alkali syndrome, adrenal insufficiency, vitamin A intoxication.

The pathophysiology of PHPT is associated with a loss of homeostatic control of PTH synthesis and secretion, leading to increased PTH secretion by individual cells or increased proliferation of parathyroid cells, but with each cell secreting normal levels of PTH. In conditions such as parathyroid hyperplasia, an increased number of parathyroid cells maintains their normal sensitivity to calcium, whereas in parathyroid adenomas, parathyroid cells show a lower than normal sensitivity to the inhibitory action of calcium. Both conditions give rise to PHPT and can lead to hypercalcemia.[4] The main target organs of PTH are the bones and kidneys. PTH is a central regulator of bone homeostasis, through its action on bone-forming osteoblasts, osteocytes, and osteoclasts.[5] In patients with PHPT, chronically elevated PTH levels cause bone loss mediated by the receptor activator of nuclear factor-κβ ligand (RANKL, also known as TNFSF11), osteoporosis and fragility fractures.[6] In the kidney, PTH stimulates tubular calcium reabsorption and phosphate excretion and stimulates 1α-25-hydroxyvitamin D hydroxylase

activity. When patients with PHPT develop hypercalciuria, the filtered calcium load is greater than the capacity of the kidneys to reabsorb calcium efficiently, even under the influence of PTH.[7]

PHPT is usually (>90%) sporadic and is caused by a solitary benign adenoma (85-90%), multiglandular involvement consisting of multiple adenomas or hyperplasia of all four glands (5-10%), and very rarely parathyroid carcinoma (<1 %).[7]

In recent years, most patients are diagnosed when they have complaints such as nephrolithiasis, bone pain, or bone deformity. Most patients with primary hyperparathyroidism are asymptomatic, diagnosed when hypercalcemia is incidentally discovered on laboratory examination. Patients usually have a history of kidney stones, bone pain, myalgia or muscle weakness, depressive symptoms, use of thiazide diuretics, calcium products, vitamin D supplements, or other symptoms associated with various etiologies of hypercalcemia. The physical examination of patients with primary hyperparathyroidism is usually normal. However, physical examination can be helpful in finding abnormalities that may suggest another etiology of hypercalcemia. Parathyroid adenomas are rarely palpable on physical examination, but the presence of a large, firm mass in the neck of a patient with hypercalcemia should raise the suspicion of parathyroid carcinoma.[8] The patient had pain in the right waist that radiated to the thigh and worsened with walking or other activities. When walking, the patient feels weak and pain in both knees. The patient's pain has been felt since 2 years ago and has gotten worse in the last 3 months. The patient is also often tired since the last month and feels loss of appetite.

Laboratory-visible hypercalcemia is the most common early sign of hyperparathyroidism. In most patients, the hypercalcemia is mild and may even be intermittent and is usually less than 1.0 mg/dL above the upper limit of normal. The PTH level should then be measured, and it may be elevated or even within normal limits. Twenty-four hour urine calcium may also be measured, but is not essential for diagnostic purposes.[9] Laboratory evaluation should include measurement of serum phosphate, renal function tests and measurement of serum 25-hydroxyvitamin D in addition to PTH and calcium. Serum phosphate levels are usually low in severe PHPT and within the lower normal range in milder forms of PHPT. In the patient underwent laboratory examination, PTH levels were found to be 455.8 pg/mL in which this patient had increased levels of parathyroid hormone, calcium levels were 13.5 mg/dL where there was an increase in calcium levels 3.2 mg/dL, potassium 2.80 mmol/dL. L where there is a decrease in potassium levels, creatinine 2.6 mg/dL and urea 64.9 mg/dL where in both markers there is an increase, which means there is a disruption in kidney function.

Indications for ultrasound based on the American Institute of Ultrasound in Medicine (AIUM) published in 2013 and jointly developed by the American College of Radiology, Society of Pediatric Radiology, and Society of Radiologists in Ultrasound, define the indications for

ultrasound of the parathyroid glands, i.e. a complementary evaluation of the incidental findings detected in other modalities, patients with primary hyperparathyroidism (mainly to determine the location of pre-operative lesions), follow-up in operated patients, evaluation of recurrence in operated patients. In hyperparathyroidism due to adenoma, the usual ultrasound appearance is typically oval or bilobed, well-defined, dense, homogeneous and hypoechoic in relation to normal thyroid tissue. The hypoechoic appearance is due to its high cellular content and low fat tissue content, which are characteristics that offer the greatest sensitivity for the detection of parathyroid adenomas.[11]

The patient also needs to be examined for other related organs, such as the kidneys and bone density. Bone turnover markers can be elevated, to what extent can be a function of the severity of bone disease. Imaging studies of the kidneys with ultrasound, X-ray or CT should be performed to detect the presence of kidney stones or nephrocalcinosis. Measurement of BMD by dual energy X-ray absorptiometry should be performed on the lumbar spine, hip (total pelvis and femoral neck) and distal third of the radius in all patients with PHPT. Depending on availability, additional tests such as the trabecular bone score or HRpQCT may be helpful.[10]

Excess calcium in the urine may result from increased intestinal calcium absorption, increased bone calcium mobilization, or both. Increased renal calcitriol production with intestinal calcium hyperabsorption is believed to be of clinical importance. Symptomatic kidney stones can be diagnosed early and symptomatic severe hypercalcemia is usually recognized late in the disease course. Excess calcium in the urine may result from increased intestinal calcium absorption, increased bone mobilization of calcium, or both. Increased renal calcitriol production with intestinal calcium hyperabsorption is believed to be of clinical importance. Primary hyperparathyroidism is associated with an increased risk of kidney stones more than 10 years before the diagnosis is made. Parathyroidectomy was associated with an 8.3% reduction in the risk of kidney stones.[13] The patient underwent ultrasound examination of the abdomen, found multiple hyperechoic lesions on the right and left kidneys measuring 6 – 12 mm with the impression of nephrolithiasis with a differential diagnosis of nephrocalcification. There was also an increase in echogenicity in both kidneys with diffuse parenchymal changes in both Brenbridge 2 kidneys, which is often seen in patients with PHPT. Another examination performed by the patient was a urological CT scan without contrast, multiple calcifications were found in both kidneys with a differential diagnosis of nephrocalcinosis and multiple cysts in the left kidney.

The gold standard for parathyroid localization is single-radioisotope scintigraphy with technetium-99m (99mTc) combined with single-photon emission computed tomography (SPECT) imaging. SPECT is a 3-dimensional sestamibi scan that improves the visualization of the parathyroid glands. This combination of methods has a 91 to 98% sensitivity for identifying

parathyroid adenomas. Four-dimensional CT and MRI have also been used in parathyroid imaging, but their sensitivity is only 75% and 40% to 85% respectively.[9]

For therapy, bilateral 4-gland exploration is the procedure of choice for hyperparathyroidism. However, because a single adenoma accounts for 85% of cases of primary hyperparathyroidism, minimally invasive parathyroidectomy is emerging as the gold standard for parathyroid adenomas.[12] Parathyroidectomy is recommended for symptomatic and asymptomatic patients who meet one of the following criteria, i.e. age <50 years, serum calcium concentration 1 mg per dl above the upper normal limit, T-score at or below 2.5 in the lumbar spine, femoral spine, total hip or distal third of the radius, or presence of vertebral fracture on X-ray or assessment of vertebral fracture, Creatinine clearance <60 ml per minute, increased risk of kidney stones by biochemical stone risk analysis, and kidney stones or nephrocalcinosis by abdominal radiograph. The patient is currently undergoing Percutaneous nephrolithotomy (PCNL) to remove multiple calcifications found in the right and left kidneys. PCNL is usually performed with the patient in the prone position through the posterior calyx with a high success rate and acceptable morbidity.[14] PCNL is a minimally invasive procedure to remove kidney stones larger than 2 centimeters. A small incision of about 1.3 cm is made in the back over the affected kidney and a pathway is made from the skin to the kidney. It is then enlarged using a series of Teflon or bougie dilators. After that, the nephroscope is inserted; Smaller stones can be removed with the aid of a device with a basket on the tip while a Holmium laser lithotripter, ultrasonic probe or electrohydraulic can break up larger stones. After removing the stone, a catheter is placed to drain the urinary system and a nephrostomy tube is placed to drain fluid from the kidney into the drainage bag.[15] The procedure on this patient is begin with a Marker that is made on the neck as the margin of the operation which is then incised according to the marker that has been made then deepened to make a flap so it separates the pratracheal muscles after that, the left thyroid is identified and the thyroid artery is ligated and it is continued with the preservation of the recurrent laryngeal nerve, then the left thyroid and isthmus are removed together.[16]

CONCLUSION

PHPT is a disorder of the parathyroid glands in which there is excessive secretion of PTH from one or more parathyroid glands which ultimately causes hypercalcemia. The most common manifestation is the discovery of stones in the kidneys, as well as a decrease in bone density. To diagnose, it is necessary to carry out laboratory tests such as PTH, calcium, and phosphate levels in the blood. Abdominal ultrasound and CT-scan of the abdomen also need to be done to determine the location of stones in the kidney. For management, minimally invasive parathyroidectomy can be performed as the gold standard for parathyroid adenomas. In addition

to parathyroidectomy, therapy for manifestations in the other organs, such as nephrolithiasis, is also still performed as an adjunct therapy.

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