Recurrent Bilateral Staghorn Stones as a Manifestation of Primary Hyperparathyroidism due to Parathyroid Adenoma

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Figure 1. Stones from the urinary tract

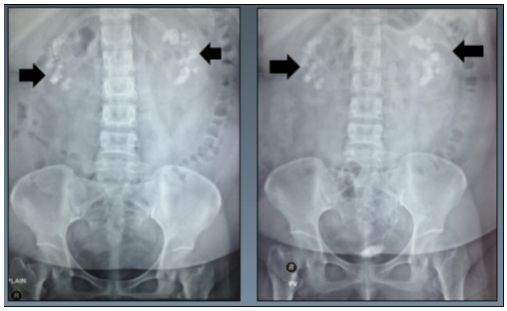

Figure 2. Intravenous pielography examination: plain (left) and post-voiding (right) show bilateral staghorn stones

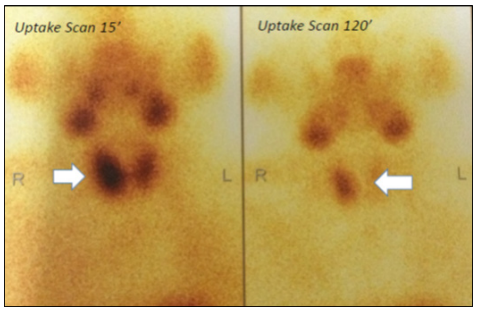

Figure 3. Parathyroid scan (99mTc-MIBI, 15 mCi) show over-radioactivity (uptake) of lower right parathyroid gland

Figure 4. Parathyroid SPECT/CT show adenoma of the lower right parathyroid gland

Primary hyperparathyroidism is a medical condition caused by overactive of parathyroid gland.[1] It is most commonly caused by solitary adenoma of the parathyroid gland.[1,2] Other causes of this condition are hyperplasia, multiple adenomas, and parathyroid cancer.[1] Primary hyperparathyroidism has some metabolic consequences in the calcium metabolism.[1-3] Hypercalcemia in patient with primary hyperparathyroidism will resulted to the most important comorbidity that is chronic deposition of calcium in the kidney forming nephrolithiasis or other urolithiasis.[3] It is not uncommon, patient with parathyroid adenoma come to health care professionals with the chief complain of recurrence nephrolithiasis.[1,4]

Nephrolithiasis develop from metabolic abnormalities or anatomic malformations of the urinary tract and infection.[4] Around 10-20% of nephrolithiasis cases are form in staghorn type. According to Amaro CRP et al.[4], staghorn calculus is the most severe presentation of urinary tract lithiasis, therefore they need further metabolic investigations in the case of staghorn stones. Study reported that hypercalciuria are the most common characteristics in staghorn calculus and investigation for hypercalcemia need to be explored.[3,4] Unfortunately, study reported the under-investigation and underestimation of further metabolic investigation for staghorn calculus. Shortly, further metabolic investigation is important to prevent the recurrency of staghorn calculus.[4]

Primary hyperparathyroidism and malignancy are responsible for more than 90% of all cases of hypercalcemia.[5] Assadi F stated that hyperparathyroidism is associated with lower serum calcium levels (<12 mg/dL) and longer duration of hypercalcemia (more than 6 months) compared to malignancy. Parathyroid hormone assay is the most useful test for differentiating hyperparathyroidism from malignancy and other causes of hypercalcemia.[5] While adenoma of parathyroid gland is suspected, examination with 99mTc-MIBI SPECT/CT is the next step for diagnostic purpose.[6]

This is a classic and good case to learn about recurrent staghorn calculus/stones, hypercalcemia, hyperparathyroidism, and adenoma of the parathyroid gland. A 28 year-old female came with the complaint of recurrent bilateral retroperitoneal pain. She was also complaining of stones excretion in the urine (**Figure 1**). From intravenous pielography examination, there was a bilateral staghorn calculus in both (right and left) kidneys (**Figure 2**). She had a history of recurrent staghorn stones in the past five years. She had experienced surgery, three times ESWL (extracorporeal shock wave lithotripsy), and PCNL (percutaneous nephro-lithotripsy) by urologic surgeon, but the bilateral stones always recur in the evaluation.

From the physical examination, the patient was obese, with costovertebral angle tenderness in the right and left (bilateral) sides, and positive ballotement test. Other organs revealed in the normal condition from physical examination. From laboratory examination, there was hypercalcemia with calcium serum 12.3 mg/dL (normal range 8.4 to 102 mg/dL). For further metabolic investigation for hypercalcemia, we perform test of parathyroid hormone assay and we get hyperparathyroidism with parathyroid hormone 344.3 pg/mL (normal range 15-65 pg/mL). Other laboratory examinations (peripheral blood, kidney, and liver function) in the normal range.

From the neck ultrasound (cervical ultrasonography), we found no abnormalities and the investigation was continued with parathyroid scintigraphy with 99mTc-MIBI scan by SPECT/CT. From parathyroid scan, the patient has adenoma in the lower right parathyroid gland. The patient was consulted to oncologic surgeon to undergo parathyroidectomy. Ten days after surgery, parathyroid hormone was decreased from 344.3 pg/mL to 106.9 pg/mL (normal range 15-65 pg/mL) and serum calcium was decreased to 10.2 mg/dL. From histopathology examination the adenoma was classified as benign (hyperplastic of the parathyroid gland). Post-parathyroidectomy, the patient was planned to undergo surgery, ESWL, and PCNL for the rest of the recent staghorn stones.

Primary hyperparathyroidism is a common metabolic disorders that affect calcium metabolism resulting hypercalcemia.[1,2,7] It has female preponderance.[7] The patient usually come

to health care fasilities with nephrolithiasis or urolithiasis and bone disease (osteoporosis).[1,7] In many cases, hyperparathyroidism can be found incidentally from screening of calcium serum.[7]

Primary hyperparathyroidism differ from secondary hyperparathyroidism.[1] Chronic kidney disease is the most common cause of secondary hyperparathyroidism which the hypocalcemia occur first following the deficiency of 25-hydroxy-vitamin D and 1.25 dihydroxy-vitamin D, inducing hyperactivity of parathyroid glands. Secondary hyperparathyroidism then increase the reabsorption of calcium ion and calcitriol synthesis. High turn over of the bone will resulted to decrease of bone mineral density and increase the risk of pathologic fractures.[8] It is noted to always check kidney function test to exclude secondary hyperparathyroidism from chronic kidney disease.[1] Other causes of secondary hyperparathyroidism must be excluded which are the use of thiazide diuretics and lithium, vitamin D deficiency, bisphosphonates, and also genetic cause such as familial hypocalciuric hypercalcemia.[1]

There are only few guidelines on the management of primary hyperparathyroidism. A scientific statement from Brazilian Society for Endocrinology and Metabolism suggested the examination of serum calcium, parathyroid hormone assay, vitamin D, and serum creatinine, renal ultrasound, and bone mineral densitometry of the lumbar spine, femur, and distal 1/3 radius by dual energy X-ray absorptiometry (DXA) for work up of hyperparathyroidism.[1] From a survey of 421 physicians in Europe consisting of endocrinologists, rheumatologists, internists, and urologists who managed primary hyperparathyroidism, majority will check parathyroid hormone, serum calcium, serum creatinine, and 24-hours urinary excretion of calcium for diagnostic tests used for patients suspected to primary hyperparathyroidism.[7]

Imaging procedure options to find the abnormalities in the parathyroid glands are cervical ultrasonography (neck ultrasound), computed tomography, magnetic resonance imaging, 99mTc-MIBI (sestamibi) scintigraphy, and PTH measurement in nodule aspiration fluid (fine needle aspiration).[1] In recent years, 99mTc-MIBI (sestamibi) single-photon emission computed tomography and computed tomography scintigraphy (SPECT/CT) have routinely used to detect adenoma and malignancy (cancer) of the parathyroid glands.[6] Our patient underwent 99mTc-MIBI (sestamibi) scintigraphy by SPECT/CT after she highly suspected as having primary hyperparathyroidism from laboratory examination. From the scintigraphy and SPECT/CT, she are known to have single adenoma of parathyroid gland with the location in the lower right gland. In the **Figure 3** and **Figure 4** we can see high uptake of the radioactive 99m Tecnetium in one of the four parathyroid glands.

Parathyroidectomy is the treatment of choice for patients with symptomatic primary hyperparathyroidectomy.[1,2] Several indications for surgery in asymptomatic primary hyperparathyroidism are serum calcium >1 mg/dL above upper limit of normal, creatinine clearance <60 mL/min/1.73 m^2, T-score <2,5 at the lumbar spine, hip, and/or distal radius or previous fragility fracture, age <50 years, and patients whose medical monitoring is not possible.[1] Our patient has recurrence bilateral staghorn stones which classify her as having symptomatic primary hyperparathyroidectomy. The benefit of parathyroidectomy are summarized by the Brazilian Society for Endocrinology and Metabolism statement, which are improved bone mineral density result, decreased risk of fractures, reduced risk of nephrolithiasis, and improved quality of life.[1] Our patient underwent parathyroidectomy of the lower right gland. After surgery, parathyroid hormone decreased dramatically from 344.3 pg/mL to 106.9 pg/mL (normal range 15-65 pg/mL), followed by decreased of the serum calsium to 10.2 mg/dL. It will also decreased the risk of future stones formation in the kidney and urinary tract.

Monitoring of parathyroid hormone, serum calcium, and clinical symptoms of the staghorn stones are mandatory for all patients after parathyroidectomy. Phamacological treatment can be indicated for patients with contraindications for surgery, surgical failure, and those with no current indication for surgery.[1] Several drugs for primary hyperparathyroidism are cinacalnet hydrochloride which is calcimimetic agent that

binds to calcium-sensing receptor of parathyroid cells and decresed PTH secretion, selective modulators of estrogen receptors (SERM) such as raloxifene, and biphosphonates such as alendronate.[1]

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