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# PRIMARY HYPERPARATHYROIDISM. A CLINICAL OBSERVATION

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**ABSTRACT** — Background. Primary hyperparathyroidism is an endocrine disease resulting from a primary pathology of the parathyroid gland, characterized by increased secretion of parathyroid hormone and increased blood calcium levels. Among the endocrine diseases, primary hyperparathyroidism is the third most common after diabetes mellitus and thyroid disease. Without timely diagnosis, primary hyperparathyroidism causes systemic damage to internal organs: renal impairment, nephrolithiasis, esophageal affection, cardiovascular and nervous system and affects bones.
The aim of the work was to present a clinical case of a patient with primary hyperparathyroidism and to analyze the stages of its diagnosis and treatment.
Material and methods. We reviewed the relevant literature and analyzed the patient's medical records.
Results and Discussion. The patient had a complicated course of primary hyperparathyroidism of bone and visceral form. Despite of the slow progression and availability of screening methods, hyperparathyroidism was detected at the stage of complications. The efficacy of the therapy has been assessed. The underlying reasons that made it difficult to diagnose PHPT at an early stage, before the development of serious complications of internal organs were investigated.
Conclusions: It can be assumed that our clinical case will increase the awareness of physicians, especially therapists, about the primary manifestations of this pathology and the challenges of its detecting and avoiding diagnostic errors.

**KEYWORDS** — primary hyperparathyroidism, parathyroid gland adenoma, hypercalcemia, parathyroid hormone, bone and visceral form.

## INTRODUCTION

Primary hyperparathyroidism (PHPT) is an endocrine disease resulting from underlying disease of the parathyroid gland, characterized by increased secretion of parathyroid hormone and high blood calcium levels [1], which leads to increased osteolysis and calcium release from bone tissue, as well as increased intestinal calcium absorption. As a result, hypercalcemia, hypercalciuria, and hyperphosphaturia develop [2]. Among endocrine diseases, PHPT is the third most common after diabetes mellitus and thyroid disease [1]. Its incidence increases with aging; women suffer 2 times more often than men; the average age of diagnosis is 54–59 years [4].

Hypercalcemia is dangerous because it has a negative effect on all systems in the body and entails dysfunction of the kidneys (nephrolithiasis, hypecalciuria), the digestive system (nausea, vomiting, constipation, peptic ulcer of the stomach, or duodenal ulcer), cardiovascular system (tachycardia, arterial hypertension, arrhythmias), nervous system (hyporeflexia, muscle weakening, headache, drowsiness, depression) [2].

The first diagnostic step on the way to a diagnosis is to identify hypercalcemia, then to determine the PTH level, calciuria, as well as niveau diagnosis, including ultrasound examination of the parathyroid glands, computed tomography of the neck and mediastinum with contrast enhancement, and scintigraphy [1].

Currently, surgical intervention is the most effective method of treatment with a low risk of complications [1].

Despite the high prevalence of the disease and the availability of information about PHPT, patients with this pathology receive ineffective treatment for years due to misinterpretation of symptoms that mask the true cause of the condition.

*The objective of the research* is to demonstrate a clinical case of a patient with PHPT, and, using this example, to analyze the stages of the disease diagnosis and treatment.

## MATERIALS AND METHODS

The authors have reviewed the medical literature on the problem of diagnosis and treatment of PHPT, as well as medical records of a female patient with this pathology.

## RESULTS AND DISCUSSION

Patient Sh., born on 07.07.1982 (38 years old). On October 28, 2020 she was admitted to the Parathyroid Gland Pathology Unit of the National Medical Research Center of Endocrinology in Moscow (Russia) by referral of Tver Regional Clinical Hospital (Russia) to choose further treatment management.

On admission, the patient complained of recurrent convulsions, paresthesia and pain in the lower extremities, pain in the lower extremities while walking for a long time. History of the disease states the first

symptom of the disease was periodical convulsions in the lower extremities which appeared in 2005, and decreased during therapy with vitamin D analogs (alfacalcidol at a dose of 0.25 μg per day). For 10 years, the patient was not observed by either an endocrinologist or a therapist. The general state was satisfactory. In 2016, she was diagnosed with urolithiasis and bilateral nephrolithiasis. In 2017, she was diagnosed with secondary chronic pyelonephritis, which in 2018 was complicated by an abscess of the right kidney. The patient was urgently operated on.

Since 2020, the patient underwent magnetic resonance imaging of the spine in connection with an episode of an acute pain syndrome in the thoracic spine while tilting the trunk, which showed a visible mass in the cervical region. According to the results of the study, she was examined by an endocrinologist with the first suspect of PHPT.

On an outpatient basis, the patient was diagnosed with hypercalcemia (total calcium — 2.76 mmol/l, ionized calcium — 1.49 mmol/l), a low level of vitamin D (46.4 nmol/l), a tenfold increase in blood parathyroid hormone (76.7 pmol/l ). On September 10, 2020, scintigraphy of the parathyroid glands revealed scintigraphic signs of adenoma of the lower right parathyroid gland. On September 15, 2020, osteodensitometry determined the total T criterion at the level of the femoral neck equal to 1.0; at the level of the lumbar spine — 0. Kidney ultrasound examination found diffuse changes in the renal parenchyma and signs of bilateral nephrolithiasis.

To decide on further management and referral to a specialized institution outside the Tver Region for surgical treatment, the patient was admitted to the specialized endocrinology unit of Tver Regional Clinical Hospital.

Positive family history of cardiovascular diseases and kidney stone disease.

During inpatient examination, a complete blood count revealed no pathology. Laboratory tests showed a slight decrease in GFR (73 ml/min and phosphorus — 0.70 mmol/L), an increase in total (2.74 mmol/L) and ionized calcium (1.50 mmol/L). The decrease in GFR was consistent with the development of such kidney complications as stage 2 chronic kidney disease. Thyroid hormone examination: free T-4 — 10.0 pmol/l, TSH — 1.50 mIU/l; free T-3 — 6.8 pmol/L, that is, free T-3 was above the norm, the rest were within its limits. Esophagogastroduodenoscopy (EGDS) revealed no pathology of the esophagus, stomach and first parts of the duodenum. Ultrasound of the thyroid gland revealed diffuse changes in the thyroid tissue with the presence of nodes in both lobes of the thyroid gland. TI-RADS 3. Scintigraphy revealed a parathyroid adenoma.

According to the results of the examination, the patient was diagnosed with primary osteo-visceral hyperparathyroidism.

The patient started treatment with Cholecalciferol 5000 IU daily. On the background of therapy, the patient had no significant changes in her state of health.

On October 2, 2020, the patient was admitted to the parathyroid gland pathology unit of National Medical Research Center of Endocrinology in Moscow, to decide on further management and possible surgical treatment.

During the examination, all values of complete blood count were within normal limits. Blood chemistry, 05.11.2020: total calcium — 2.79 mmol/l (hypercalcemia), albumin — 44 g/l, albumin-adjusted calcium — 2.71 mmol/l. Blood PTH, 28.10.2020 is significantly increased and amounts to 295.8 pg/ml. Common urine analysis — 1016, acidic reaction, no protein, leukocytes 2–3 in the field of view, no bacteria. Electrocardiogram within normal limits.

Considering the young age of the patient and periodic rises in blood pressure to exclude the hereditary nature of PHPT, an extended examination was carried out: insulin-like growth factor-1 — 244.9 ng/ml, cortisol of evening saliva — 2.31 nmol/ml, daily urine — 137 nmol/day, aldosterone-renin ratio — 58.7 (pg/ml). Evaluation of the indicators found a high level of insulin-like growth factor-1, while the rest of the indicators were within normal limits. The daily urinary calcium excretion was 12.1275 mmol/day, which was almost 2 times higher than the standard. Ultrasound examination of the thyroid and parathyroid glands revealed sonographic signs of multinodular goiter with focal changes, EU-TIRADS 2, signs of adenoma of the right lower parathyroid gland. Densitometry of the right proximal femur: -0.8; lumbar spine: -0.4; and distal radius: -2.0. Contrast-enhanced multispiral computed tomography of the neck, abdomen, and retroperitoneal space revealed signs of adenoma/hyperplasia of the parathyroid gland in the lower third of the neck, signs of multinodular goiter, enlarged liver and spleen, and a cystic mass in S4 liver. There were calculi in the calixes of both kidneys, signs of postischemic changes in the right kidney.

Based on the history, clinical findings, laboratory and instrumental results, the patient was clinically diagnosed with: Primary diagnosis: Primary osteo-visceral hyperparathyroidism. A mass lesion of the right parathyroid gland. Complications of the underlying disease: Recurrent urolithiasis, bilateral nephrolithiasis, chronic secondary pyelonephritis, non-acute. Chronic kidney disease, stage 2. Osteopenia (low mineral density -2.0 SD by Z-criterion) of the radius.

Concomitant diseases: Multinodular colloid goiter, 1 degree (WHO), euthyroidism. Liver cyst.

Surgeon consultation, 05.11.2020: a 38-year-old patient with confirmed primary hyperparathyroidism (albumin-adjusted calcium — 2.81 mmol/l, PTH — 295.8 pg/ml, calcium in daily urine 12.1 mmol/day), a mass lesion of the right lower parathyroid gland 2.8x0.9x0.8 cm. Indications for scheduled surgical treatment.

Prior to the scheduled operation, on 02.11.2020 the patient started treatment with a calcium mimetic drug to lower the PTH level — Cinacalcet, 30 mg, evenings. The patient was discharged from the hospital on 05.11.2020 in a satisfactory condition, with improvement, under the local outpatient supervision of specialists. Recommendations for the continuation of drug therapy with Cinacalcet 30 mg once a day, evenings; after 1 month, testing of laboratory parameters, namely, total blood calcium, ionized, albumin, phosphorus, creatinine, PTH, followed by consultation with an endocrinologist, at least once every 3 months. The patient needs to receive the results of a genetic test (MENI). Recommendations for routine surgical treatment of primary hyperparathyroidism in a specialized endocrinological hospital in 2–3 months.

Analyzing this clinical case, we should note that a total of 15 years passed from the onset of early primary manifestations of the disease (2005) to the diagnosis of complicated hyperparathyroidism. Late diagnosis of the disease prevented the patient from receiving effective therapy before the complications developed. The burdened family history of kidney stone disease could somewhat confuse the doctors and be also the reason for the late diagnosis. It can be assumed that the search for the cause of the development of kidney stone disease would allow to diagnose PHPT a little earlier.

During the examination, the clinicians should have to consider the complaints (periodic cramps in the lower extremities) and the relationship of their relief with the course of taking vitamin D, to timely conduct laboratory tests to confirm the diagnosis of PHPT, namely to determine the blood level of PTH and calcium. An additional examination: to determine the level of vitamin D, perform densitometry, kidney ultrasound, EGDS has to be performed.

After the diagnosis, it was necessary to adjust the diet to limit calcium intake to 800–1000 mg/day and increase fluid intake to 1.5–2.0 l/day. [3]. Then, monitor the following parameters: the level of calcium in the blood — 2–4 times a year; blood creatinine, GFR — 1 time in 6 months, PTH — 1 time in 6 months; daily excretion of calcium in the urine — 1 time in 6 months; ultrasound of the kidneys — once a year; measurement of BMD in the radius, femur, vertebrae; lateral radiographs of the spine with suspected fractures of the vertebral bodies (decreased growth, the appearance of back pain); EGDS — once a year [1]. In the case of indications, prompt surgical treatment is indicated — selective parathyroidectomy.

It can be assumed that the parathyroidectomy will significantly improve the condition of the patient. At the same time, she will still need to monitor the state of bone tissue and kidneys by an endocrinologist, urologist and nephrologist. Timely nephroprotective therapy will slow down the progression of chronic kidney disease.

## CONCLUSIONS

Late diagnosis of PHPT in the patient at the stage of severe complications indicates a lack of awareness among practitioners about the pathogenesis of hyperparathyroidism, the variety of its clinical signs and options for screening examination. It can be assumed that raising the awareness of primary care specialists about the features of diagnosis and treatment of PHPT will allow timely identification of this pathology and effective therapy, before the development of serious complications.

*Conflict of Interest Statement:*

The authors declare no conflict of interest.

*Author Contributions:*

*Danila Vasiliev* — literature review, text writing. *Anastasia Kulish* — research design, text writing; *Olga Poselyugina* — collection and processing of materials, research concept, editing; *Elena Andreeva* — literature review, editing.

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