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Parathyroid adenoma in a 15-year-old girl with recurrent urolithiasis

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ABSTRACT

Introduction and aim. The incidence of urolithiasis in children has been growing steadily for several decades, and it accounts for an increasing percentage of hospitalizations. Kidney stones are deposits of various mineral salts. Most of them are composed of calcium, favored by hypercalcemia and hypercalciuria. Primary hyperparathyroidism is one of the reasons for increased calcium levels in the blood.

Description of the case. A 15-year-old girl was hospitalized due to recurrent urolithiasis. Investigations revealed hypercalcemia with elevated parathyroid hormone. Ultrasound of the thyroid gland showed a local change near the lower pole of its right lobe, and Sestamibi nuclear scan confirmed the presence of the adenoma of the lower right parathyroid gland. Surgical removal of the parathyroid gland with the present adenoma was performed. Calcium and phosphate homeostasis parameters and the kidneys' ultrasound image were without any significant deviations from the norm.

Conclusion. After finding the cause of recurrent urolithiasis, the applied surgical treatment resolved all disease manifestations.

Keywords. primary hyperparathyroidism, urolithiasis, pediatrics, hypercalcemia, kidney stones

The list of abbreviations:

PHPT – primary hyperparathyroidism, **PTH** – parathyroid hormone, **SPECT** – single-photon emission computed tomography, **FHH** – familial hypocalciuric hypercalcemia, **HPT-JT** – hyperparathyroidism jaw tumor syndrome, **XLHP** – X-linked hypophosphatemia

Introduction

The incidence of urolithiasis in children has been growing steadily for several decades and accounts for an increasing percentage of hospitalizations.[1-8] The etiology of the formation of kidney stones is not fully understood. The risk of urolithiasis seems to be higher among boys in the first decade of life and girls in the second decade, i.e., during puberty, which suggests the role of reproductive hormones.[3,4] Kidney stones are deposits of various mineral salts, most of which are composed of calcium, favored by hypercalcemia and hypercalciuria.[8] Ultrasound is the initial imaging method in diagnosing urolithiasis disease in children.[4,9]

Aim

We present a case of a 15-year-old girl hospitalized due to hypercalcemia in the course of recurrent urolithiasis.

Description of the case

Within a year and a half, the girl was hospitalized three times due to periodic symptoms of renal colic. Previously used antispasmodics and analgesic drugs resulted in rapid resolution of colic, and the girl was discharged home.

According to anamnesis, she has not reported any problems with the digestive system, denied pain in the bone and joint system, fatigue, and hyperhidrosis. In the family history, the patient's uncle had two episodes of urolithiasis disease, patient's brother is healthy. The parents of our patient performed the blood test with the parameters of the calcium phosphate homeostasis - both of them were found to have elevated levels of parathyroid hormone (PTH) (mother: 90.8 pg/mL, father: 123 pg/mL) with slightly lowered vitamin D level (mother: 24 ng/mL, father: 20 ng/mL). Both parents had normal calcium (mother: 9.2 mg/dL; father: 9.7 mg/dL) and phosphorus (mother: 3.1 mg/dL; father: 2.7 mg/dL) levels and did not agree to extend the diagnostics.

The girl was repeatedly admitted to the hospital with abdominal pain and vomiting. In physical examination, she presented moderate abdominal tenderness with right-sided positive Goldflam's sign.

Laboratory tests showed an increased level of calcium and creatinine in the blood, with a slightly elevated level of these parameters in the daily urine sample. Abdominal ultrasound showed deposits in both kidneys with size 3-4 mm. Additionally, in the right kidney, dilatation of the pyelocalyceal system with urinary retention and dilation of the right ureter was seen. The patient was consulted by a urologist who did not find indications for surgical intervention.

After the applied treatment (antispasmodics and analgesic drugs), the deposits in the kidneys were excreted. Due to the recurrent nature of the ailments, the diagnostics were extended – high levels of parathyroid hormone were found with simultaneous normal thyroid hormone levels (TSH, FT4), vitamin D deficiency,

persistently elevated levels of calcium and creatinine in the blood, phosphorus and cystatin C levels were normal. In the daily collection of urine, there was hypercalciuria and low tubular phosphate reabsorption which proved hyperphosphaturia. The most relevant patients' blood and urine test results are shown in Table 1.

Table 1. Patients' blood and urine test results

	Patient's test results	**Reference value**
Serum creatinine	1.33 mg/dL	0.24–0.73 mg/dL
Serum calcium	12.84 mg/dL	9.12–10.2 mg/dL
Serum phosphates	3.3 mg/dL	2.9–5.1 mg/dL
Vitamin D	18.62 ng/mL	30–100 ng/mL
Parathyroid hormone	351 pg/mL	18.5–88.0 pg/mL
Ionized calcium	1.53 mmol/L	1.15–1.33 mmol/L
Alkaline phosphatase	180 U/L	70–370 U/L
Creatinine in 24-hr urine collection	25.52 mg/kg/24h	16–30 mg/kg/24h
Calcium in 24-hr urine collection	4.98 mg/kg/24h	1–4 mg/kg/24h
Tubular Reabsortion of Phosphate (TRP)	83.64%	85–89%
Cystatin C	1.11 mg/L	0.64–1.23 mg/L

Ultrasound examination of the thyroid gland revealed a focal change near the lower pole of its right lobe. Due to the ambiguous image, a reactive lymph node or parathyroid adenoma was suspected. The performed parathyroid single-photon emission computed tomography (SPECT) confirmed the presence of an adenoma of the lower right parathyroid gland (Fig. 1)

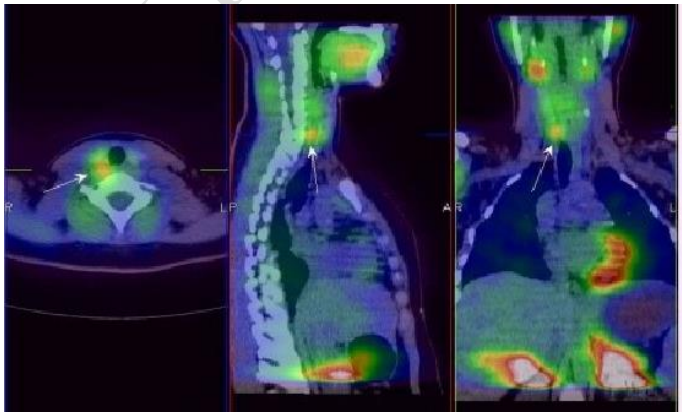

Fig. 1. Scintigraphic examination of the parathyroid glands (planar + SPECT/CT). The arrow marks the focus of intense Technetium (99mTc) sestamibi uptake in contact with the lower pole of the right thyroid lobe

In order to exclude the presence of MEN1 and MEN2a syndromes, in subsequent studies, the levels of prolactin, CEA, blood chromogranin A, urinary catecholamines, and methoxy-catecholamines have been measured, and no abnormalities were found. The circadian rhythm of cortisol was maintained. Slightly elevated levels of insulin and C-peptide were found with a normal glycemic profile. A genetic test for the syndromes mentioned above was not performed in our patient.

The patient was administered for parathyroidectomy (Fig. 2A-B).

Intraoperatively, the level of parathyroid hormone was measured twice (before – 317.9 pg/mL and after the right lower parathyroidectomy) – about 20 minutes after the removal of the gland, the level significantly decreased (34.8 pg/mL), which confirmed the excision of the right parathyroid gland. The course of the operation and the postoperative period were uneventful. Control blood levels of calcium and parathyroid hormone were normal. Histopathological examination of the sample confirmed the presence of an entirely removed parathyroid adenoma (Fig. 2C).

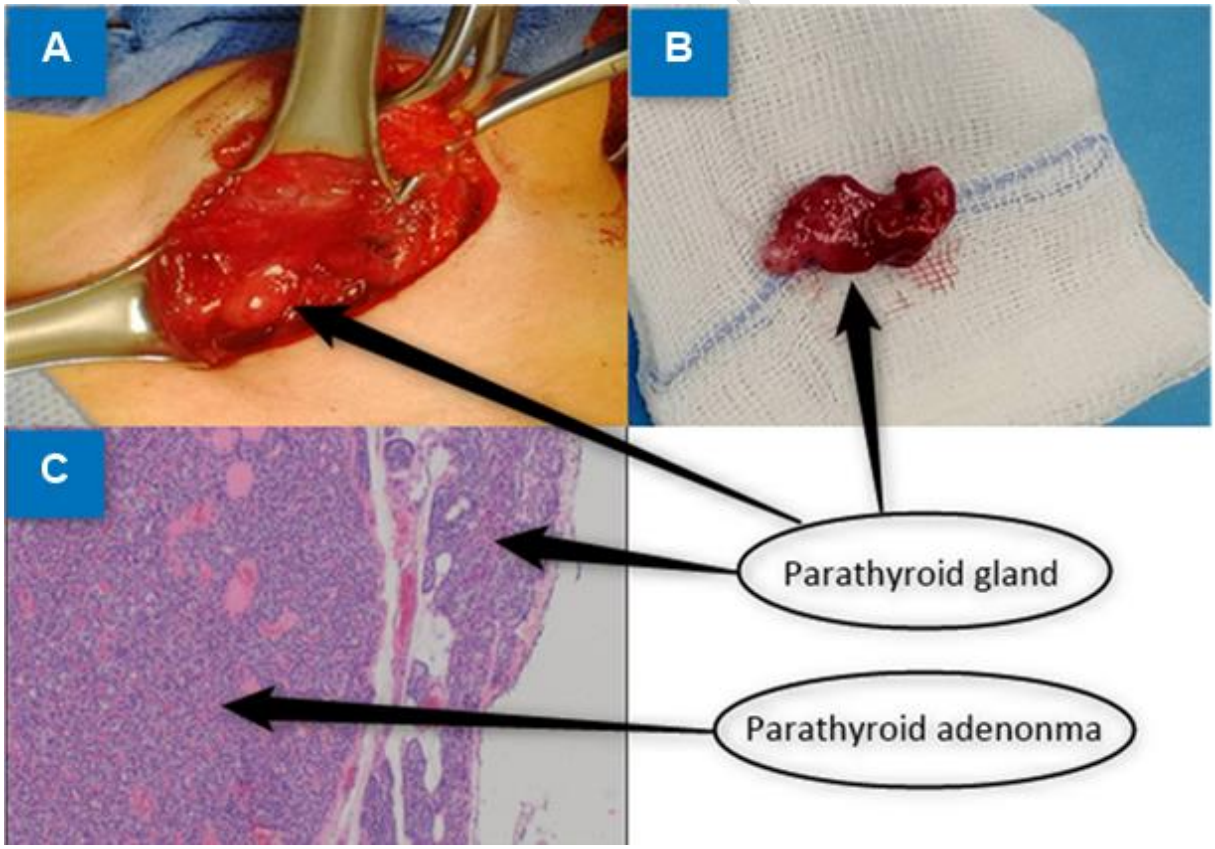

Fig. 2. (A) Intraoperative picture of adenoma and parathyroid removal from the cervical access; (B) Removed right inferior parathyroid gland with adenoma; (C) Histopathological picture of the normal parathyroid gland with adenoma at 40 times magnification

Bone densitometry, performed one month after the operation, revealed the results within limits expected for age and gender. During the follow-up visit, approximately two months after the operation, calcium and phosphate homeostasis were checked: normocalcemia (10 mg/dL), normophosphatemia (3.4 mg/dL), and decreased vitamin D levels (18 ng/mL) were found. Slightly elevated parathyroid hormone (120.6 pg/mL), renal parameters, and ions in a single urine portion were within normal limits. The ultrasound image of the kidneys revealed no deposits, urine retention or dilatation of the pyelocalyceal system. In the postoperative field, no pathological structures (except the fibrous scar) were visualized within the thyroid gland. The patient started vitamin D supplementation and currently remains under the supervision of the Endocrinology and Nephrology Clinic.

Discussion

Primary hyperparathyroidism (PHPT) in young patients is much less common than in adults, with an estimated incidence of 2–5 per 100,000.[10] Its most common cause is a single parathyroid adenoma (65-70%). More rarely, hyperparathyroidism may be a manifestation of multiple neoplasms of the endocrine glands (MEN 1 or 2a) or rare syndromes of familial isolated hyperparathyroidism. So far, parathyroid carcinoma has been described in 20 patients in the pediatric population.[11]

All clinical symptoms of PHPT are associated with the excessive production of parathyroid hormone, which leads to disturbances in calcium and phosphate homeostasis.[12,13] The laboratory indicator of the changes taking place in the organism is hypercalcemia. Clinical manifestations of persistently elevated blood calcium levels may be atypical to the underlying disease, i.e., eating disorders, weight loss, apathy, chronic abdominal pain, nausea, vomiting, bone and joint pain, muscle weakness, polyuria, polydipsia, depressed mood, difficulty concentrating, headaches. The above issues cause a delay in making a correct diagnosis, leading to the consolidation of complications in internal organs. Usually, the patient has abnormalities in one system (60%).[10]

Primary hyperparathyroidism can lead to urolithiasis (like in the case of our patient), as well as to nephrocalcinosis, intensifies bone metabolism, which may result in early osteoporosis, increased susceptibility to fractures and bone deformities (such as valgus knee or osteitis fibrosa cystica).[10,13,14] Hypercalcemia can affect the heart muscle, causing vascular, myocardial, and valvular calcifications, left ventricular hypertrophy, and arrhythmia. It also leads to arterial hypertension and increases the risk of myocardial infarction and stroke.[15,16] The essential element in diagnostics is looking for complications, which most often concern the osteoarticular and excretory systems. In order to determine the condition of

the skeleton, the level of alkaline phosphatase is determined, and the bone morphology is assessed using the densitometric method. It is also important to assess kidney function with the blood markers such as creatinine, cystatin C and estimated glomerular filtration rate. In the case of symptoms of hyperparathyroidism in the form of urolithiasis, an ultrasound examination of the urinary system and 24 hour urine collection should be performed to determine the excretion of calcium, phosphate, uric acid, oxalate, citrate, and cysteine.[17] Ultrasound examination of the urinary system also makes it possible to assess nephrocalcinosis. Nephrocalcinosis refers to abnormal calcium deposits within the tubulointerstitial tissue of the kidney.[18]

Considering that PHPT is the most characteristic feature of the MEN1 syndrome and may be the first related pathology, the presence of other syndrome components should be excluded, including mainly tumors of the anterior pituitary gland and pancreatic islets. For this purpose, the levels of prolactin, chromogranin A, insulin, and peptide C were measured in our patient. Less often, primary hyperparathyroidism may appear as an element of MEN2a manifestation, including medullary thyroid carcinoma and pheochromocytoma. Therefore, the level of catecholamines and methoxy-catecholamines in urine and CEA in blood serum were determined.[19] Since both parents had elevated levels of PTH, genetically determined disorders i.e., familial hypocalciuric hypercalcemia (FHH), hyperparathyroidism jaw tumor syndrome (HPT-JT), or X-linked hypophosphatemia (XLHP) should be considered. FHH was excluded because the patient's Calcium-Creatinine-Clearance-Ratio was 0.014 (<0.01: FHH is likely). HPT-JT is a rare genetic disease characterized by ossifying fibroma of the maxilla and/or mandible. XLHP is less likely because of the X-linked inheritance and normal level of phosphorus in both parents blood. In addition, its initial clinical symptoms usually appear in the first two years of the patient's life. Predominant manifestations include deformation, usually of lower extremities, and growth disturbances.[20] As the deficiency of the vitamin D is the most common cause of disrupted parathyroid hormone levels, it was considered to be the reason of the patient's parents abnormal blood test results.

In diagnosing hyperparathyroidism, imaging tests are aimed at locating the lesion before surgery. The standard methods include neck ultrasound and single-photon emission computed tomography.[14,17,21]

The surgical treatment is the 'gold standard' therapy of primary hyperparathyroidism in the pediatric population in the case of symptomatic course and the presence of organ lesions in this group of patients.[13,14] Currently, minimally invasive parathyroidectomy techniques are used in most cases. A helpful tool for assessing the procedures' effectiveness is the Miami criterion: if the concentration of PTH in the blood collected 10-20 minutes after the lesion removal decreases by 50% of the baseline value, it proves the success of the surgery.[11,17] After surgery, most patients (75%) may experience transient hypocalcemia and hypophosphatemia – the so-called hungry bone syndrome.[11] In specialized centers, the effectiveness of surgical treatment is 90%.[22]

Conclusion

In the described case, after finding the cause of recurrent urolithiasis, the applied surgical treatment resolved all disease manifestations.

Declarations

Funding

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Author contributions

Conceptualization, P.K., K.DG., R.P., P.B. and B.K.; Methodology, P.K. and K.DG.; Formal Analysis, P.K. and K.DG.; Investigation, P.K., K.DG., and B.K.; Resources, R.P., and P.B.; Writing – Original Draft Preparation, P.K., K.DG.; Writing – Review & Editing, P.K., K.DG, B.K.; Visualization, K.DG..; Supervision, B.K.

Conflicts of interest

Authors declare no competing interests.

Data availability

The data may be made available to interested persons at the request of the corresponding author via e-mail.

Ethics approval

All subjects gave informed consent to the inclusion prior to participating in the study.

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