ВТОРИЧНЫЙ И ТРЕТИЧНЫЙ ГИПЕРПАРАТИРЕОЗ ПРИ ХРОНИЧЕСКОЙ БОЛЕЗНИ ПОЧЕК

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Цели лечения вторичного гиперпаратиреоза у пациентов с хронической болезнью почек направлены на предотвращение прогрессирования заболевания и подавление активности околощитовидных желез с помощью модуляции рецепторов к витамину D и кальций-чувствительных рецепторов. Однако возможности терапии ограничены при тяжелом течении гиперпаратиреоза; моноклональные изменения и узловая трансформация желез с потерей рецепторов к витамину D и кальцию формируют резистентность к указанной терапии с развитием медикаментозно неуправляемого гиперпаратиреоза. В связи с чем формируется когорта пациентов, нуждающихся в хирургическом лечении. У этих пациентов, даже после проведения успешной трансплантации почки не происходит нормализация минерально-костных нарушений и наблюдается персистенция гиперпаратиреоза с развитием третичного гиперпаратиреоза с гиперкальциемией и гипофосфатемией. Паратиреоидэктомия является эффективным методом лечения тяжелого гиперпаратиреоза, резистентного к медикаментозной терапии.

В статье представлен результат собственного длительного наблюдения и комплексного подхода к лечению различных форм гиперпаратиреоза (вторичный и третичный) у пациента с хронической болезнью почек (5 стадия, заместительная почечная терапия программным гемодиализом и состояние после проведения аллотрансплантации почки). Обсуждаются сложности диагностики и возможности многокомпонентной терапии минерально-костных нарушений при хронической болезни почек на примере клинического случая. Продемонстрировано, что только комплексный подход к проблеме может дать положительный эффект медикаментозного лечения вторичного гиперпаратиреоза, но при развитии персистирующего третичного гиперпаратиреоза после аллотрансплантации почки показана паратиреоидэктомия.

КЛЮЧЕВЫЕ СЛОВА: *Клинический случай; вторичный гиперпаратиреоз; третичный гиперпаратиреоз; цинакальцет; паратиреоидэктомия; гемодиализ; трансплантация почки*

SECONDARY AND TERTIARY HYPERPARATHYROIDISM IN CHRONIC KIDNEY DISEASE

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In the treatment of secondary hyperparathyroidism of end-stage chronic kidney disease, vitamin D receptor activation and allosteric modulators of the calcium-sensing receptor – inhibit glandular hyperplasia, reduce parathyroid hormone levels, impact on bone turnover and mineral density. But the use of calcimimetic and vitamin D analogs or mimetics did not reduce the need for parathyroidectomy for refractory hyperparathyroidism. The enlarged parathyroid gland and gland nodular transformation became refractory to medical therapy and patient need for parathyroidectomy. Tertiary hyperparathyroidism is a state of excessive secretion of parathyroid hormone after a long period of secondary hyperparathyroidism and renal transplantation.

In this article, we present the case of a Caucasian male with chronic kidney disease (end-stage on chronic hemodialysis and after kidney transplantation) and different forms of hyperparathyroidism (secondary and tertiary). Our case study shows that only a multi-interventional strategy is likely to be more effective treatment in cases of severe and refractory to medical therapy hyperparathyroidism.

KEYWORDS: *Case report; secondary hyperparathyroidism; tertiary hyperparathyroidism; cinacalcet; parathyroidectomy; hemodialysis; kidney transplantation*

BACKGROUND

Currently, chronic kidney disease (CKD) is considered as a multidisciplinary medical problem rather than just a nephrological condition. Renal replacement therapy (dialysis) and kidney transplantation are considered complementary in the treatment of ESRD (end-stage renal disease). A loss in the number of functioning nephrons in CKD causes a complication cascade, including vitamin D deficiency, hyperphosphatemia, changes in calcium-sensing receptor (CaSR) function in the parathyroid glands (PTG), lower gastrointestinal absorption of calcium, increased synthesis of parathyroid hormone (PTH), hypertrophy and hyperplasia of PTG cells. Such hyperplasia involves PTG cell transformation accompanied by aggressive growth and reduced vitamin D receptor and CaSR expression [1, 2].

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Subjected to a timely initiated treatment, secondary hyperparathyroidism (SHPT) in most patients can be controlled by dietary phosphorus restrictions and pharmacotherapy (phosphate-lowering agents, vitamin D oral or parenteral formulations, calcimimetics) [3-5]. However, there is a cohort of patients resistant to the aforementioned therapy despite the achieved success in the conservative treatment of CKD and clear criteria for prescribing and monitoring. Even after successful kidney transplantation these patients still have mineral bone disorder and persistent hyperparathyroidism with a consequent development of tertiary hyperparathyroidism (THPT) accompanied by hypercalcemia and hypophosphatemia. In a large-scale observational retrospective study 18% of patients (108 out of 607 patients) were diagnosed with elevated PTH levels and 8% (47 patients) had hyperparathyroidism with hypercalcemia both within the first year after successful kidney transplantation [6]. Parathyroidectomy is an effective treatment of secondary and tertiary hyperparathyroidism resistant to the drug therapy [7]. A described case report demonstrates the challenges in disease management and the need for timely diagnostics of the mineral bone disorder and its complications in patients with CKD. It is also a relatively rare example of SHPT transition which was successfully treated prior to the kidney transplantation into tertiary hyperparathyroidism (THPT) occurred after the allotransplantation, thus leading to parathyroidectomy.

CASE REPORT

Patient M., born in 1966, with stage 5 CKD on kidney replacement therapy (chronic hemodialysis), sought medical attention at the Endocrinology Research Centre of the Ministry of Healthcare of the Russian Federation in 2009.

At the time of encounter the patient complained about muscle weakness, bone and joint pain, stiffness in body movements, and skin pruritus.

Past medical history shows periodic disease (familial Mediterranean fever) in 1976 and kidney amyloidosis in 1988 according to biopsy. Stage 5 CKD was diagnosed in 2006; the patient was put on kidney replacement therapy (chronic dialysis). Above symptoms began to trouble patient in 2008. After examination the patient was diagnosed with CKD-mineral bone disorder (CKD-MBD): secondary hyperparathyroidism with PTH level of 634 pg/mL. Since that time the patient irregularly received treatment with vitamin D active metabolites (Alfacalcidol 4 μg a week). In 2008 a cadaveric kidney allotransplantation resulted in acute rejection. A tendency for increased calcium-phosphorus product has been observed since 2009.

After the patient encounter the following lab tests were performed:

- *PTG ultrasound* have revealed signs of four parathyroid glands hyperplasia; upper right: V = 1.08 mm3, lower right: V = 0.04 mm3, upper left: V = 0.3 mm3, lower left: d = 0.6 cm.
- Wrist X-ray showed vascular calcification (3rd stage) and active nail bone resorption.

Table 1. Laboratory results on the first admission

Test	Value
Total calcium (mmol/l)	2,53
Phosphorus (mmol/l)	2,1
Albumin (g/l)	42
PTH (pg/ml)	816,1
Alkaline phosphatase (IU/l)	496
Osteocalcin (ng/ml)	over 300
C-terminal telopeptide (CTx) (ng/ml)	3,1
25(OH)D (ng/ml)	7,9
TSH (μIU/mL)	2,1
Hemoglobin (g/l)	90-105 (during EPO therapy)

- *Bone densitometry* showed a decrease (Z-score) in bone mineral density (BMD) in the lumbar spine (L1-L4) down to -1.1 SD; in the proximal femur (total hip) down to -2.2 SD; in the femoral neck (neck) down to -2.0 SD; in the radial bone (Rad 33%) down to -4.0 SD.

Laboratory test results are shown in the table 1.

Clinical diagnosis: CKD-MBD (stage 5) as a result of kidney amyloidosis (chronic dialysis since 2006, condition after the kidney transplantation and acute graft rejection in 2008): secondary hyperparathyroidism with hyperplasia of the four parathyroid glands, hyperphosphatemia, vitamin D deficiency, decreased (Z-score) bone mineral density of mixed origin (CKD, hyperparathyroidism) down to -4.0 SD in the radial bone, nail bone subperiosteal resorption in both wrists, extraskeletal calcification.

COMMENT: It should be mentioned that patients with stage 3-5D CKD have increased bone fragility due to both decreased bone mineral density and deterioration of bone microarchitecture (with normal and increased mineral density). Taking this information into account and considering pathophysiological differences, the term "osteoporosis" should be used only at early stages of CKD; a consequent decrease in mineral density should be described as "chronic kidney disease-mineral bone disorder with decreased bone mineral density" [8].

The following **therapy was recommended**, based on the results of the clinical examination:

1. for secondary hyperparathyroidism correction - cinacalcet, 30 mg/day;
2. for hyperphosphatemia relief - strict hypophosphate diet (not more than 800 mg per day) and prolongation of chronic dialysis sessions;
3. for target calcemia maintenance according to Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease (KDOQI, 2.13-2.37 mmol/L) - decrease in calcium concentration in the dialysis solution down to 1.25 mmol/L.

Levels of PTH, serum calcium, serum albumin, and serum phosphorus were checked monthly.

During follow-up period:

1. the cinacalcet dose was titrated up to 60 mg per day;
2. to correct vitamin D deficiency Colecalciferol (50,000 IU/week) was added to the therapy after the phosphorus level was back to normal;

3. after vitamin D deficiency has been corrected (36 ng/mL), alfacalcidol was added to the therapy (1 μg three times a week) in order to correct SHPT, providing normal levels of calcium and phosphorus along with PTH levels over 300 pg/mL (KDOQI, 2003).

During 6 weeks of the combination therapy, a positive dynamics of health parameters was observed:

- **Clinical data**: fewer complaints, no skin pruritus.
- **Laboratory data**: PTH level decreased by 60.2%, [Ca] x[P] product decreased by 22.03%. Bone-formation (AP, OC) and bone-resorption (CTx) marker levels decreased, vitamin D deficiency was compensated.

Instrumental methods of examination

- *Wrist X-Ray* showed a decrease in vascular calcification (to stage 2), and fewer signs of nail bone resorption.
- *Densitometry* showed a prominent positive dynamics: in the L1-L4 up to +5.4%, in total hip up to +6.4%, in neck up to +4.9%, and in Rad 33% up to +9.3%.
- *PTG ultrasound* revealed a reverse in hyperplasia of three (!) PTGs, but an increase in the right upper PTG volume, i.e. V=1.89 mm3 (+75%).

COMMENT: Therefore, improvement was achieved during the combination therapy. The dynamics and range of decrease in lab test values generally depend on the PTG hyperplasia type (diffuse, nodular, or combined). Nodular hyperplasia development is accompanied by certain drug therapy resistance. According to the literature and our findings cinacalcet and vitamin D formulations inhibit PTG cell proliferation and decrease their activity, also decrease both hyperplasia and volume of the glands providing there was no nodular transformation [9, 10]. The nodular hyperplasia is defined by such surrogate criteria as a maximum size (over 1 cm in diameter) or volume (over 0.5 cm3) of the gland according to the ultrasound examination [9, 10].

Our case report evidences that PTGs with the initial volume less than 1 mm3 decreased in size and were not detected in the control test, whereas the gland over 1 mm3 increased in size.

On May 27, 2010, the cadaveric kidney allotransplantation was repeated. The graft had primary function, the induction immunosuppressive therapy included basiliximab injections at 40 mg doses, the basic therapy included a calcineurin inhibitor (tacrolimus: starting dose 0.13-0.18 mg/kg/day, then according to drug plasma levels monitoring), mycophenolate (1.0-1.5 g/day), prednisolone (30 mg/day with a consequent dose titration down to the maintenance dose of 5-10 mg/day).

After the calcium-phosphorus metabolism has been normalized due to the conservative treatment, the connection with the patient was lost. The patient sought medical attention again after the kidney transplantation in August 2010. According to the patient, cinacalcet was discontinued right after the transplantation but he received another drug product which exerts the effects on the calcium-phosphorus metabolism, i.e. alfacalcidol 4 μg/week.

Laboratory results on 11.08.2010 are shown in table 2.

- *PTG ultrasound* demonstrated only the right upper PTG which increased up to V = 2.1 mm3.

Clinical diagnosis: CKD-MBD (T1) as a result of kidney amyloidosis (chronic dialysis in 2006-2010, condition after the kidney transplantation and acute graft rejection in 2008, condition after the repeated kidney transplantation on May 27, 2010, graft function is satisfactory): tertiary persistent hyperparathyroidism with hyperplasia of the upper right parathyroid gland, hypercalcemia, vitamin D deficiency, osteoporosis of mixed origin (CKD, hyperparathyroidism, steroid-induced) with a loss in bone mineral density down to Z-score -3.4 SD in the radial bone.

Table 2. Laboratory results on August 2010

Test	Value
Creatinine (μmol/l)	69
GFR (mL/min/1.73m2)	98
Total calcium (mmol/l)	3.4
Phosphorus (mmol/l)	0.98
Albumin (g/l)	39
PTH (pg/ml)	815
Alkaline phosphatase (IU/l)	416
25(OH)D (ng/ml)	22.7

COMMENT: As mentioned earlier, successful kidney transplantation does not always lead to recovery from mineral bone disorder. Some graft recipients demonstrate persistent hyperparathyroidism or tertiary hyperparathyroidism accompanied by hypercalcemia and hypophosphatemia [6]. Development of nodular PTG hyperplasia is a common cause of such hyperparathyroidism. Taking into account the volume of the upper right PTG, a parathyroidectomy was required prior to the kidney transplantation. No specific recommendations for management of patients with THPT after the kidney transplantation are available so far. However, persistent hypercalcemia is an indication for an active therapeutic intervention like in every case of hyperparathyroidism.

Initial recommendations in this case include:

1. maximum limitation in the food which contains calcium;
2. correct water schedule;
3. alfacalcidol withdrawal;
4. cinacalcet 60 mg/day with dose titration.

During cinacalcet dose titration a tendency for PTH and calcium blood level decrease was observed; however, parameters were outside a normal range (table 3).

COMMENT: It should be mentioned that the PTH target level corresponds to that in the general population whereas the graft function is adequate. The main aim of cinacalcet treatment is the normalization of calcium-phosphorus metabolism parameters. A decrease in the PTH concentration correlates with the cinacalcet concentration. However, due to nodular PTG hyperplasia and a decrease in CaSR number and sensitivity, along with a decrease in vitamin D receptors number and sensitivity, the gland becomes resistant to the drug therapy [9, 10]. Parathyroidectomy is a treatment of choice in PTG drug resistance.

A suspected nodular transformation of PTG cells led to a decision to perform parathyroidectomy.

On October 11, 2010, parathyroidectomy (the upper right PTG) was performed.

PTH levels were monitored during the surgery in order to assess performance of the intervention. Such

Table 3. Changes in blood calcium and PTH levels during Cinacalcet dose titration

Cinacalcet dosage (mg)	PTH (ph/ml)	Blood calcium (mmol/l)
60	576	2,9
120	403	2,68
180	298	2,54
210	313	2,51
240	282,4	2,56

procedure is usually carried out in the treatment of primary hyperparathyroidism, however, taking into account similarities between primary and tertiary condition, it can be used in hyperparathyroidism after the kidney transplantation. PTH blood level rapidly decreases after the surgery, if no other hyperplastic PTGs are present. If in 10-15 minutes after parathyroidectomy the PTH level decreased two-fold or more (comparing to the maximum lever prior to the surgery), the second hyperfunctional PTG in the patient is quite unlikely. A rapid PTH level decrease means that the surgery can be finished and there is no need to remove all PTGs [11, 12].

15 Minutes after parathyroidectomy PTH levels decreased more than 50% which evidences an adequate PTG removal.

Histological examination of the PTG revealed nodular hyperplasia in the chief cells.

COMMENT: An active bone tissue recovery takes place after parathyroidectomy accompanied by the hungry bone syndrome (increase in AP versus baseline and marked hypocalcemia). Hypocalcemia can be quite evident in patients with severe renal hyperparathyroid osteodystrophy.

In the postoperative period the patient experienced marked hypocalcemia (clinical and laboratory evidence), so he received high doses of calcium carbonate products (4 g/day) and vitamin D active metabolites (3 μg/day) with gradual dose down-titration until a complete withdrawal (March 2011). Blood calcium, PTH, and AP levels were controlled during the whole period.

COMMENT: The literature sources discuss a functional state of the kidney graft in patients after parathyroidectomy. According to several authors, there is an increase in serum creatinine levels [13], however, other researchers prove otherwise: the surgery has no effects on the creatinine level increase and worsened function [14].

The graft function of our patient was stable and satisfactory, no significant changes in creatinine levels were observed (table 4).

Densitometry showed a decrease in BMD: in the L1-L4 down to -1.0 SD; in the total hip down to -2.2 SD; in the neck down to -2.0 SD; and in the Rad 33% down to -3.2 SD.

Clinical diagnosis: CKD-MBD (T1) as a result of kidney amyloidosis (chronic dialysis in 2006-2010, condition after the kidney transplantation and acute graft rejection in 2008, condition after the repeated kidney transplantation on May 27, 2010, graft function is satisfactory): condition after parathyroidectomy (the right upper PTG) due to persistent tertiary hyperparathyroidism, vitamin D deficiency, osteoporosis of mixed origin (CKD, hyperparathyroidism, steroid-induced) with a loss of bone mineral density down to Z-score -3.2 SD in the radial bone.

Table 4. Laboratory results on April 2011

Test	Value
Creatinine (μmol/l)	71
Total calcium (mmol/l)	2.21
Phosphorus (mmol/l)	1.1
Albumin (g/l)	43
PTH (pg/ml)	34
25(OH)D (ng/ml)	27.3

COMMENT: According to the clinical recommendations on CKD-MBD if the renal graft function is satisfactory, osteoporosis treatment should be started within 12 months after the kidney transplantation. The drug therapy is the same as in general population and depends on the CKD stage [8, 15].

According to the recommendations, both the correction of vitamin D deficiency and anti-osteoporotic therapy were initiated (alendronate, a bisphosphonate drug in tablets). During the follow-up, calcium-phosphorus metabolism parameters (blood and daily urine) and the graft function were within normal ranges.

Densitometry in 2012, 2013, and 2014, showed positive dynamics. According to the bone densitometry in 2014 no decrease in BMD was observed in the lumbar spine, in the proximal femur and in the femoral neck; the only BMD decrease was found in the radial bone (an early stage of osteopenia). Therefore, a decision on a medication-free period has been made, with the next assessment of BMD 1 year apart.

The patient has received only colecalciferol 10,000 IU/week.

After the patient sought medical attention in July 2016, a high PTH level (71 pg/mL), vitamin D deficiency (21.4 ng/mL), and serum creatinine 98 μmol/L with normal levels of calcium and phosphorus in the blood and urine were detected.

Densitometry showed a decrease in BMD: in the total hip down to -1.8 SD; in the neck down to -1.7 SD; in the Rad 33% down to -1.6 SD. No decrease in BMD was observed in the L1-L4.

Vitamin D formulations (both active and inactive forms) and dynamic monitoring **were recommended** after patient examination.

CONCLUSION

The described case report clearly demonstrates how complicated the management of CKD-MBD patients can be.

The drug therapy (vitamin D and calcimimetic) of SHPT during CKD in dialysis stage provides prominent positive dynamics with the normalization of calcium-phosphorus metabolism parameters, improvement of hyperparathyroid renal osteodystrophy progression, BMD recovery and decrease in bone turnover markers. During the complex treatment a reverse of hyperplasia and/or hypertrophy of three PTGs was observed; the fourth gland, however, increased in volume which was an indirect sign of PTG nodular transformation and monoclonal growth.

Development of hypercalcemia during persistent THPT is relatively rare providing a successful SHPT treatment at the dialysis stage and an adequate function of the kidney graft after its transplantation. Our clinical report is an example of SHPT transition (successfully treated prior to the kidney transplantation) to THPT (after the kidney allotransplantation) which proves the importance of both laboratory tests and PTG volume evaluation before the kidney transplantation. Despite calcemia stabilization and a tendency for PTH level decrease during calcimimetic therapy, a decision to perform parathyroidectomy was made due to suspected PTG nodular hyperplasia which was later confirmed by histology. Marked hypocalcemia was observed at the postoperative period due to the hungry bones syndrome. Normalization of calcium-phosphorus metabolism parameters was observed after the syndrome compensation. Kidney graft function was stable and satisfactory, no significant creatinine level changes or worsened function were observed after parathyroidectomy and during dynamic follow-up. The anti-osteoporotic therapy demonstrated good results in BMD increase.

Despite complicated management of CKD patients with different forms of hyperparathyroidism, a personalized combination approach therefore proves to be successful.

ADDITIONAL INFORMATION

Conflict of interests. Authors declare no explicit and potential conflicts of interests associated with the publication of this article.

The patient's informed consent. The patient provided his informed consent for the publication of this case report.

СПИСОК ЛИТЕРАТУРЫ | REFERENCES

1. Abe M, Okada K, Soma M. Mineral Metabolic Abnormalities and Mortality in Dialysis Patients. *Nutrients*. 2013;5(3):1002-1023. doi: 10.3390/nu5031002.
2. Goodman WG, Quarles LD. Development and progression of secondary hyperparathyroidism in chronic kidney disease: lessons from molecular genetics. *Kidney Int.* 2008;74(3):276-288. doi: 10.1038/sj.ki.5002287.
3. Chertow GM, Dillon M, Burke SK, et al. A randomized trial of sevelamer hydrochloride (RenaGel) with and without supplemental calcium. Strategies for the control of hyperphosphatemia and hyperparathyroidism in hemodialysis patients. *Clin Nephrol*. 1999;51(1):18-26.
4. Chertow GM, Lu ZJ, Xu X, et al. Self-reported symptoms in patients on hemodialysis with moderate to severe secondary hyperparathyroidism receiving combined therapy with cinacalcet and low-dose vitamin D sterols. *Hemodialysis International*. 2012;16(2):188-197. doi: 10.1111/j.1542-4758.2011.00642.x.
5. Block GA, Martin KJ, de Francisco ALM, et al. Cinacalcet for Secondary Hyperparathyroidism in Patients Receiving Hemodialysis. *N Engl J Med.* 2004;350(15):1516-1525. doi: 10.1056/NEJMoa031633.
6. Bleskestad IH, Bergrem H, Leivestad T, Gøransson LG. Intact parathyroid hormone levels in renal transplant patients with normal transplant function. *Clin Transplant.* 2011;25(5):E566-E570. doi: 10.1111/j.1399-0012.2011.01515.x.
7. Егшатян Л.В., Рожинская Л.Я., Кузнецов Н.С., и др. Лечение вторичного гиперпаратиреоза, рефрактерного к альфакальцидолу, у пациентов, получающих заместительную почечную терапию программным гемодиализом // Эндокринная хирургия. – 2012. – Т. 6. – №2. – С. 27-41. [Egshatyan LV, Rozhinskaya LY, Kuznetsov NS, et al. The treatment of secondary hyperparathyroidism in haemodialysis patients' refractory to alfacalcidol. *Endocrine Surgery*. 2012; (2):27. (In Russ)]. doi: 10.14341/2306-3513-2012-2-27-41.
8. Kidney Disease: Improving Global Outcomes CKDMBDWG. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl*. 2009(113):S1-130.
9. Komaba H, Nakanishi S, Fujimori A, et al. Cinacalcet Effectively Reduces Parathyroid Hormone Secretion and Gland Volume Regardless of Pretreatment Gland Size in Patients with Secondary Hyperparathyroidism. *Clin J Am Soc Nephrol.* 2010;5(12):2305-2314. doi: 10.2215/cjn.02110310.
10. Егшатян Л.В. Эффективность терапевтического и хирургического лечения вторичного гиперпаратиреоза у пациентов, получающих заместительную почечную терапию программным гемодиализом: Дис. ... канд. мед. наук. – Москва; 2012. [Egshatyan LV. *The effectiveness of therapeutic and surgical treatment of secondary hyperparathyroidism in patients on chronic hemodialysis*. [dissertation] Moscow; 2012. (In Russ).]
11. Dowthwaite SA, Young JE, Pasternak JD, Yoo J. Surgical Management of Primary Hyperparathyroidism. *J Clin Densitom*. 2013;16(1):48-53. doi: 10.1016/j.jocd.2012.11.006.
12. Lambert LA, Shapiro SE, Lee JE, et al. Surgical treatment of hyperparathyroidism in patients with multiple endocrine neoplasia type 1. *Arch Surg.* 2005;140(4):374-382.
13. Lee PP, Schiffmann L, Offermann G, Beige J. Effects of Parathyroidectomy on Renal Allograft Survival. *Kidney Blood Press Res.* 2004;27(3):191-196. doi: 10.1159/000079810.
14. Schlosser K, Rothmund M, Maschuw K, et al. Graft-dependent Renal Hyperparathyroidism Despite Successful Kidney Transplantation. *World J Surg.* 2008;32(4):557-565. doi: 10.1007/s00268-007-9337-3.
15. Eknoyan G, Levin A, Levin NW. Bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis.* 2003;42:1-201. doi: 10.1016/s0272-6386(03)00905-3.

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