WHAT DO WE KNOW ABOUT SECONDARY HYPERPARATHYROIDISM

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History

In 1879, Sandström was the first to describe in man small structures adhering to the posterior surface of the thyroid capsule. At that time, they were no longer anonymous, since in 1852, parathyroid glands were described in the animal kingdom by Sir Richard Owen, who autopsied a rhinoceros. In 1891, von Reklinghausen reported a disease entity which he called „osteitis fibrosa cystica”, but relating the condition to a disease of the parathyroids had to wait till 1904, when Ashkanazy described bone damage in a patient with a parathyroid tumor. In 1908, W. G. MacCallum and Carl Voegtlin were the first investigators to suspect that hypocalcemia and other presently identified symptoms of hypoparathyroidism following thyroidectomy were associated with resection of the parathyroids rather than with thyroid resection itself. In 1914, Jacob Erdheim and Z. Schlagenhaüfer observed a single, enlarged parathyroid gland in a patient with osteitis fibrosa cystica, what resulted in numerous studies that culminated with the first parathyroidectomy performed by Mandel in Vienna in 1925; the patient suffered from the disease we know today as primary hyperparathyroidism. The notion of hyperparathyroidism was introduced in 1929 to describe a syndrome which included a disease of the bones, nephrolithiasis, myasthenia, hypercalcuria and hypercalcemia. In 1934, Fuller Albright was the first to describe enlargement of the parathyroids resulting from renal failure. Papenheimer and Willens supported this discovery by numerous post-mortem examinations performed in patients who died due to uremia; the authors published their observations in 1935. In view of the relatively slow development of endocrinology in the past century as compared to other medical specialties, diseases of the parathyroid gland are among the last entities to warrant a modern definition (1, 2, 3).

Subtotal parathyroidectomy was for the first time described by Stanbury in 1960. In 1975, Samuel Wells was the first surgeon to describe the technique of total parathyroidectomy combined with autotransplantation of fragments of a parathyroid gland to the brachoradial muscle. In recent years, the common trend aiming at limiting the extent of surgical trauma and employing minimally invasive methods has brought about the development of minimally invasive video assisted parathyroidectomy (MIVAP), which is most extensively used in treatment of primary hyperparathyroidism (PHPT). In the case of secondary hyperparathyroidism (SHPT), due to the necessity of exposing all the parathyroid glands, the procedure requires a highly skilled surgeon and the employment of strict criteria of patient selection, what limits its more widespread use. The value of videoscopic access to the parathyroids situated extracervically, especially within the chest, should be stressed; these procedures include videoscopic thymectomy (the parathyroids are often located within the thymus) (4-7).

Anatomy

The majority of humans have four parathyroid glands, two on each side, which adhere to the posterior surface of the thyroid capsule. Some individuals may have fewer glands (two
or three), what various sources describe as occurring in 3-19% cases, some may exhibit the presence of a higher number of parathyroids (as many as eight); this is a rare phenomenon in healthy subjects, but in patients with chronic renal failure (CRF), the percentage may be as high as 25%. The location of extra parathyroids may be varied. They may appear both at typical sites, as supernumerary and/or divided glands, or lie above or below their natural site, even descending to the mediastinum. In the seventies, an idea of parathyromatosis developed, which was believed to be responsible for numerous supernumerary glands observed in patients with CRF, while hypocalcemia, hyperphosphatemia and deficit of active vitamin D would be factors promoting this pathology (8-12).

Epidemiology

The most common causes of CRF in adults are glomerulopathies, hypertension and diabetes (each of these entities contributes more than 20% to the pathogenesis of the disease), followed by cystic kidney disease (approximately 10%), systemic kidney diseases and parenchymal nephropathies (approximately 5%), unknown and other causes, including congenital defects (approximately 10% each). In children, CRF is most often associated with the presence of congenital defects of the urinary tract. In patients with end-stage renal failure, the prevalence of PHPT is determined as 20%. The number of these patients increases with an increasing duration of the disease. The European Dialysis and Transplant Association reports that parathyroidectomies are required in 15% of patients after 10 years and 38% patients after 20 years of dialysis therapy (4, 13-18).

Pathophysiology

In spite of the fact that the compensatory abilities of the kidneys are vast and uremia develops only following the loss of approximately 80% of active nephrons, an impaired calcium-phosphate balance and vitamin D metabolism, which play the key role in the development of SHPT, occur at much earlier stages of CRF. A decrease in kidney mass in CRF leads to a decrease of the number of vitamin D particles hydroxylated to its active form, what is the most important factor triggering calcium-phosphorus metabolism (CPM) disturbances in SHPT. In addition, a decrease in the number of active nephrons leads to retention of phosphates – another of the most significant factors that evoke CPM disturbances (17, 18). Biological activity of circulating parathormone (PTH) in uremic patients is believed to be possibly significantly lower than the value resulting from iPTH determinations by classic tests. These tests were demonstrated to overestimate the concentration of biologically active hormone and - in addition to 1-84 PTH (which activates adenyl cyclase and is hence termed CAP – cyclase activating PTH) - they also react to PTH fragments that are devoid of 6 initial amino-acids, i.e. 7-84 PTH (which does not activate the enzyme and is thus called CIP – cyclase inhibiting PTH), whose activity towards 1-84 PTH is straight-out antagonistic. Physiological studies have demonstrated that the ratio of CAP/CIP oscillates around 1 under normal conditions, falls below 1 in patients with adynamic bone disease and is more than 1 in diseases with high bone turnover and metabolism. We know at present that disturbances occurring in CRF and SHPT affect not only the skeleton, and the greatest significance is ascribed to increased mortality rates in dialyzed patients due to circulatory diseases, especially when such patients present with concomitant SHPT. This is a result of vascular calcifications, especially when present in the coronary vessels, which involve the vascular muscle layer and atheromatous plaques, cardiac valves and the cardiac muscle itself, as well as to cardiac fibrosis (18, 19).

The role of calcium

The main factor that regulates PTH secretion is the concentration of ionized calcium in the extracellular fluid. Even a small drop in the concentration within seconds results in an increase of PTH secretion through changes evoked in activation of the calcium receptor (CaR) in the parathyroid cells. In addition, decreased ionized calcium levels that may persist for several hours activate transcription of pre-pro-PTH-encoding genes and increase PTH synthesis; in the case of persistent prolonged stimulation, parathyroid proliferation occurs. Calcium also triggers changes in the stability of mRNA-PTH and the balance between PTH secretion and degradation. The calcium receptor recognizes the extracellular ionized calcium level. It appears that the very expression of the receptor is regulated by active vitamin D and phosphates. A hyperplastic parathyroid demon-
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strates a poorer reaction to changes in calcium levels as compared to a normal gland and this phenomenon underlies resistance to conservative treatment in SHPT. It should be mentioned here that even in case of hypercalcemia, the level of PTH never entirely vanishes, and in the case of hyperplastic glands, the baseline secretion is increased in comparison to secretion demonstrated by normal glands, proportionally to parathyroid mass (17, 19, 20).

The role of phosphorus and the product of calcium x phosphate (CaxP)

Phosphate retention affects the development of SHPT through several mechanisms. It induces hypocalcemia, decreases the activity of D-1α hydroxylase in the kidney and thus results in decreasing serum active vitamin D levels. In addition, an increased phosphate concentration value stimulates the parathyroids to increased PTH production via regulation of gene expression and increased synthesis of mRNA-PTH (it stabilizes mRNA and facilitates translation) and also stimulates proliferation of the parathyroid cells (17, 19, 20, 21). The product of CaxP depends on the serum levels of calcium and phosphates. Calculations of its value are helpful and provide information on the increased risk of calcifications developing in the soft tissues if its value exceeds 5.6 (mmol²/l²). Although extensive soft tissue calcifications are rare, the most significant and the most dangerous phenomenon is the formation of calcium deposits in blood vessel walls (an increased CaxP product denotes an increased mortality rate of patients with CRF). Concentration values of phosphates that exceed 2.13 mmol/l exponentially increase the risk of death due to cardiovascular diseases and are an independent risk factor for death in hemodialyzed patients. For this reason, hyperphosphatemia has been termed a silent killer of patients with renal failure (19, 22, 23, 24).

The role of vitamin D

A genuine or relative deficit of vitamin D plays a significant role in the pathomechanism of SHPT. In the case of nodular parathyroid growth in SHPT, a decrease occurs in the number of specific vitamin D receptors in the gland and vitamin D resistance develops. At low vitamin D levels, the gene expression and synthesis of PTH (pre-pro-PTH) are increased, similarly as it happens in the case of calcium. Prolonged persistent low vitamin D concentration levels in patients with CRF result in hypocalcemia and its consequences (19, 20). The number of vitamin D receptors has been demonstrated to be inversely proportional to parathyroid weight and cell proliferation (25).

Parathyroid glands – stimulation and enlargement

A transient change in PTH levels depends solely on oscillations in ionized calcium values. In long-term regulation, phosphates and vitamin D add their contribution. These three factors affect parathyroid enlargement and increase PTH secretion. Already in the early stage of renal failure, the parathyroids increase in weight, their morphology and histologic structure change. Initially, the glands show a diffuse growth pattern, when histologically, polyclonal proliferation predominates. Subsequently, nodular growth is observed, involving both the chief and oxyphilic cells, what is believed to be a consequence of monoclonal proliferation, which is responsible for autonomous PTH secretion. This is why when no appropriate prophylaxis is employed, the majority of CRF patients develop SHPT. Analyzing bone tissue bioplates, it is estimated that the incidence of SHPT in patients with CRF is 70%, (15, 19, 26, 27, 28).

Skeleton

In SHPT patients, a consequence of CPM disturbances is renal osteodystrophy with a high bone turnover, but its presence - most often in the form of subperiosteal resorption of bone - may be observed in less than 50% of the patients. CRF patients may also present with a low bone turnover. Osteodystrophy manifested as adynamic bone disease has been noted in spite of elevated serum PTH levels. This is a consequence of a relative PTH deficit and resistance of bone tissue to parathormone activity. In patients with a low bone turnover, hypocalcemia develops due to low calcium absorption by bone tissue. The increasing incidence of adynamic osteodystrophy is probably also associated with excessively high calcium levels in the dialyzate, excessive supply of calcium carbonate and active vitamin D metabolites. Treatment of the condition consists in partial inhibition of PTH secretion (18, 19, 29, 30). In view of the resistance of bone tissue to PTH, to maintain a normal bone turnover, the optimum
PTH level is believed to be 2-3/4 times higher than the normal value for a healthy man (9, 21, 31). Hyperphosphatemia in patients with CRF also increases the production of hydrogen ions, what leads to metabolic acidosis and promotes bone resorption by osteoclasts (32).

Calciphylaxis

It is a rare, but highly dangerous complication of CRF treated with dialysis therapy in patients with concomitant SHPT. Calciphylaxis develops from vascular calcifications leading to necrosis of the skin, soft tissues and at times even muscles (especially affecting the lower extremities), with resultant necrosis and sepsis that are often fatal. The method of choice is then parathyroidectomy aiming at providing conditions for wound healing and infection control (33, 34).

The need for early SHPT management

The above mentioned structural and functional changes are difficult to reverse; this is why it is important to early initiate appropriate prevention and treatment of SHPT in the pre-dialysis phase of CRF (19).

PTX and kidney transplantation

Renal transplantation is the optimum and only causal treatment of patients with CRF. In patients with concomitant SHPT, PTX is performed at first in order to allow for restoration of normal CPM via overcoming the autonomous component of PTH secretion, while appropriate CPM regulation is provided by a well-functioning transplant. In case a patient has been subjected to successful kidney transplantation, but an elevated PTH level persists along with symptoms of hyperparathyroidism, the condition is termed „tertiary hyperparathyroidism”. It is most frequently observed when – following appropriate SHPT management in a patient with renal failure subsequently subjected to kidney transplantation - monoclonal growth develops in the parathyroid stump (sPTX) or in the autotransplanted parathyroid gland (tPTX+AT). Then, PTH secretion is autonomous and resistant to pharmacotherapy (35).

Parathyroid imaging studies

Preoperative localization of parathyroids is helpful in planning the surgical strategy prior to bilateral neck exploration. Methods characterized by varying levels of invasiveness are employed, starting from ultrasonography through computed tomography, magnetic resonance imaging, to determinations of iPTH levels in venous blood, and scintiscans. Ultrasonography is in this case a method with limited sensitivity, but it is, nevertheless, commonly used and non-invasive. Ultrasound examinations also allow for additional assessment of possible deposits in the soft tissues. Ultrasonographic control may be also employed in parathyroid biopsy and in administration of chemical substances to perform parathyroid ablation (calcitriol, ethanol). A surgeon experienced in using this method may perform a preoperative examination all by itself, thus obtaining information on the location of the parathyroids. Using the Power Doppler mode, one may assess the parathyroid blood supply (which increases when the parathyroid morphology changes towards the nodular form) and select the least pathological parathyroid gland (e.g. for autotransplantation) (36-40).

Scintigraphy is a more accurate method. Initially performed using two isotopes – thallium and technetium or iodine – the value of scintigraphy increased when technetium99 combined with methoxyisobutyl-isonitrile (MIBI) and the biphasic technique were introduced. The method proves absolutely correct in PHPT, with sensitivity amounting to 94%, but in the case of SHPT it is not as effective; the examination itself is more difficult, and sensitivity is around 50%. This is a consequence of a lower tracer uptake by the parathyroids as compared to adenomas in PHPT. Parathyroid scintigraphy is not useful in evaluating the number of glands while examining the patient before the first surgical procedure. Its sensitivity increases when used in imaging the glands that have not been resected during the initial PTX. The scan may be also helpful in negative selection of parathyroid glands for autotransplantation. Pulsatile calcitriol therapy within two weeks prior to scintiscan has been noted to decrease its sensitivity (41-45). New methods, such as 123I/99mTc- sestamibi subtraction scintigraphy or combining subtraction scintigraphy with single photon emission computed tomography (123I/99mTc-Se-stamibi SPECT) are particularly efficient (15, 46, 47, 48). Their sensitivity is approximately 80% (77-82%) in patients with SHPT and almost 100% in PHPT patients. In its modification (double tracer 99mTc-pertechnetate/99mTc-tetrophosmin/SPECT), the sensitivity of the method increases to almost 100% in SHPT.
Regardless of the imaging method employed, patients with SHPT demonstrate a simple, although not a linear relation – the larger the parathyroid gland, the greater the chance of its detection (47-51). On the other hand, the larger the parathyroid gland is, the higher the probability of it being resistant to conservative treatment (8, 52). In view of the lack of an optimal and highly effective method of parathyroid imaging, some authors recommend MRI, but in studies carried out to date, its sensitivity and specificity are comparable to ultrasound and do not exceed parameters characteristic of 99mTc MIBI (53, 54, 55).

Conservative treatment

Prevention of SHPT in patients with CRF and basic objectives of conservative treatment include prevention of hyperphosphatemia developing and maintenance of correct calcium levels. Prevention of hyperphosphatemia is necessary in patients with CRF for the following reasons: firstly, hyperphosphatemia is an element of SHPT pathogenesis, and secondly, when combined with elevated calcium levels in the presence of vitamin D, it promotes formation of Ca-P deposits in the soft tissues. Controlling phosphate levels is achieved by controlling dietary phosphate consumption, administration of phosphorus-binding pharmaceuticals and dialysis therapy. The physician exerts the lowest degree of influence on the diet of his patient, as it is difficult to modify nutritional habits. Aluminum-containing phosphate binders are highly effective, but they pose a danger of aluminum poisoning (the element is also naturally present in water and in some gastric mucosa protective agents), development of anemia, osteomalacia and encephalopathy; they also increase mortality rates in patients with CR. Short-term administration of such medications in order to promptly decrease phosphate levels is justified. On the other hand, pharmaceuticals, in which aluminum has been replaced with calcium, are divided into agents containing absorbable and non-absorbable calcium. Pharmaceuticals that contain absorbable calcium – in spite of benefits associated with simultaneous prevention of hypocalcemia – pose a danger of increasing the CaxP product and intensifying Ca-P depositing in the soft tissues. The risk is even greater when the patients are administered vitamin D preparations. On the other hand, modern preparations, such as sevelamer hydrochloride (an anion exchange resin, which additionally considerably slows down the process of calcification development), contain non-absorbable calcium and may be safely combined with vitamin D preparations (28, 56). A necessary element of appropriate control of the level of phosphates in patients with end-stage CRF lies in correctly planned and executed dialysis sessions. It has been demonstrated that the optimum control of phosphate levels may be achieved by overnight hemodialyses six times per week, which allow for removing up to 50% more phosphates as compared to standard therapy. Hemodialysis performed three times per week has a limited effect on phosphate levels and more than 70% of patients hemodialyzed due to CRF present with elevated serum phosphate values. Maintenance of normal serum calcium levels (normocalcemia) in patients with SHPT is implemented via prevention of hypocalcemia employing calcium preparations (or possibly absorbable calcium-containing phosphate-binding agents) and vitamin D preparations, at the same time not allowing hypercalcemia to develop. The presently employed therapeutic management is often inadequate, even leading to accelerated development of calcifications in the vascular walls and soft tissues. Various reports question the employment of traditional phosphorus-binding calcium preparations, as well as vitamin D preparations, regarding these pharmaceuticals as leading to hypercalcemia and hyperphosphatemia, yet, no uniform opinion prevails. It appears that a safer solution would be found in administration of new medications, which bind phosphates but do not contain absorbable calcium, as well as new vitamin D analogues and calcimetics (20, 29, 57, 58, 59). Calcimetics constitute a new group of pharmaceuticals, which regulate the function of the calcium receptor acting as its allosteric activator and may decrease the level of PTH by as much as 80% (20, 29, 57, 58). These agents are highly effective in patients, in whom after vitamin D therapy, the level of PTH has decreased, but the CaxP product is persistently increased. In addition, experimental studies employing calcimetics have proven their role in successful treatment of osteodystrophy. This is of particular importance since after PTX, skeletal deformations generally do not regress (19, 60).

Vitamin D analogues

New vitamin D analogues, such as doxercalciferol (an analogue of alphacalcidiol) decre-
ase PTH concentration levels, increase intestinal calcium absorption and modulate bone reconstruction – what is the most important, without triggering hypercalcemia and hyperphosphatemia. Similar activity is exhibited by oxacalcitriol, which decreases the level of PTH itself and also the concentration value of markers indicating a high bone turnover (61). Clinical trials aiming at assessing the effectiveness of vitamin D therapy depending on route (oral versus parenteral) and mode of administration (continuous versus pulsatile) have provided no firm answer; some authors have failed to observe any differences. For this reason, in various centers, various routes and modes of vitamin D administration are employed (19, 57, 58, 62, 63).

An invasive therapeutic modality in SHPT is chemical parathyroid ablation using ultrasound-controlled percutaneous ethanol injections into the gland. If the procedure is successful, the effect is comparable to surgical treatment with respect to permanence and quality. The advocates of the method point to its simplicity and selectivity, but in practice, it is employed in selected cases only in view of the limitations of visualization method. Moreover, similarly as in the case of surgery, the injection may be complicated by recurrent laryngeal nerve palsy (64-68).

A variant of the procedure is administration of calcitriol to the parathyroids; however, the glands with a relatively large size do not respond to such treatment. In view of post-injection complications occurring even after a properly performed procedure (tissue edema and necrosis, hemorrhages, adhesions), the method should not be employed as a first choice modality (64, 69, 70, 71).

When the patient does not respond to conservative treatment, surgery should be considered.

If the weight of the parathyroids exceeds 500 mg (the normal value is approximately 120 mg), one should suspect nodular proliferation and associated resistance to conservative treatment (72, 73, 74).

SURGICAL TREATMENT

Indications for PTX

Surgical treatment of SHPT is indicated by a failure of conservative treatment. Detailed indications depend on the intensity of clinical symptoms (pruritus, ostealgia, muscle weakness, soft tissue calcifications, fractures, calciphylaxis), biochemical parameters (hypercalcemia and hyperphosphatemia with concomitant high iPTH levels – according to some sources above 500-800 pg/ml, elevated CaxP product above 70 (mg/dl)^2, i.e. 5.6 (mmol/l)^2 and low calcium levels in response to elevated PTH without vitamin D deficit) and possible bone changes (decreased mineralization) (21, 75-78).

In view of muscle weakness, which according to some authors affects as many as 100% of patients with SHPT, it is suggested to recognize myasthenia as a single factor constituting and indication for surgery. It is postulated that patients with iPTH levels above 1000 pg/ml and no response to conservative treatment within 6 months should be referred to PTX (4, 22, 79, 80, 81).

The idea of the surgical procedure in patients with SHPT consists in bilateral neck exploration and visualization of all the parathyroids. Imaging studies do not provide ultimate information on the number of parathyroids in a particular patient and this is why, if fewer than four glands are visualized during the procedure, other than typical sites of parathyroid localization should be reviewed. For this reason, the preferred surgical approach is a low transverse neck incision, which also allows for exploring the region situated behind the episternum or even the region of the hyoid bone. The lateral approach allows for bypassing the well-vascularized subhyoid region and shortens the access route to the parathyroids; in case of a reoperation, it allows for dissecting the tissues situated beyond the surgical scar. While employing this approach, we should remember about the risk of damaging the ansa cervicalis with resultant paralysis of the ansa cervicalis-innervated muscles (the patients also experience a change of voice!) and about a more difficult operation should the parathyroids be situated in an anomalous region. A factor that facilitates the work of the surgeon is intraoperative iPTH monitoring, which gives an almost 100% confirmation of the appropriate extent of the procedure (5, 75, 82, 83). If no such possibility is available, the surgeon should resect the thymus and fat tissue of the central neck compartment during the procedure in order to avoid missing supernumerary parathyroids (15, 26). Access to parathyroids in SHPT may be achieved also by minimally invasive techniqu-
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es (minimally invasive video-assisted parathyroidectomy – MIVAP), but in view of the complexity of the procedure and the necessity of a strict selection of the patients, the technique is not commonly employed (7).

There are various strategies of operating on the parathyroids themselves. It is generally assumed that sPTX and tPTX + AT are employed in patients, in whom kidney transplantation is anticipated, while tPTX without AT is performed solely in patients who have not been qualified for renal transplants (26, 84). sPTX allows for leaving in situ a naturally vascularized and blood-supplied fragment of the parathyroid at the site of its normal location and basically an immediate assumption of function by the parathyroid stump. In turn, following tPTX + AT to the forearm tissues, it is possible to evaluate the function of the implanted parathyroid tissue via the comparison of parathormone concentrations in blood samples collected from both forearms (the Casanova test). In case of possible recurrent disease, the test determines whether excessive PTH secretion originates from the parathyroid transplanted into the forearm or from another site - in the majority of cases a supernumerary parathyroid (this is not possible when the gland is transplanted to the sternocleidomastoid muscle). An argument against tPTX + AT is based on the risk of parathyroid tissue dissemination not only within the site of autotransplantation, but even to remote sites of the body (no such risk is posed by sPTX). Moreover, to perform autotransplantation, one should select tissue material devoid of nodular growth in order to minimize the risk of proliferation, what requires collaboration with an experienced pathomorphologist (26, 85, 86, 87). In view of studies on late results of PTX, however, both methods, i.e. tPTX + AT and sPTX, despite their technical dissimilarities, give comparable results (2).

In the case of both the above-mentioned surgical techniques, complications may lie in fixed hypoparathyroidism. This is why when possible, a fragment of the resected material is recommended to be cryopreserved and stored for some time after the procedure (88). tPTX without AT is performed only in chronically dialyzed patients with severe SHPT who do not qualify for renal transplants. When all the parathyroids are resected, an advantage lies in no risk of recurrent disease. Although the procedure allows for controlling CPM, yet in view of the complete absence of PTH, it leads to development of adynamic bone disease and/or severe hypocalcemia and requires life-long calcium supplementation. In patients after PTX, clinical symptoms resolve promptly, ostealgia and pruritus decrease in intensity, while muscle strength increases (4, 89-92). In his investigations carried out in 2001, Chou et al. also emphasizes the improvement of sexual performance in male patients after PTX for SHPT (93).

Therapeutic failures

The necessity to reoperate most often arises from missing a supernumerary parathyroid or monoclonal proliferation of the parathyroid tissue left in situ (a parathyroid stump in the case of sPTX; in tPTX + At, proliferation is most frequently seen within the transplanted parathyroid, although disseminations of parathyroid cells to neighboring tissues or even to remote localizations also occurs (94, 95, 96). Failures in surgical treatment may be divided into two classes: persistent hyperparathyroidism, when after the operation, no PTH level normalization is achieved, and recurrent hyperparathyroidism, when after the primary drop in PTH concentration to normal values, its level increases again minimum six months postoperatively. The mean therapeutic failure rate after surgical treatment of SHPT approximates 11%, although it may be as high as 70-80%. If the procedure is executed correctly, irrespectively of the method employed, the incidence of recurrent disease due to parathyroid stump growth in case of sPTX or transplanted parathyroid cell proliferation in case of tPTX + AT ranges from 5 to 8%; however, when a missed parathyroid gland is left in situ, the percentage increases. Recurrence is in more than 90% of cases associated with nodular growth of the parathyroid fragment left in situ. The success of reoperation depends on individual parathyroid anatomy of the patient, accuracy of the employed visualization methods and above all – similarly as in the case of the primary procedure – the experience of the surgeon (15, 16, 84, 85, 95, 97).

In patients, in whom autonomous parathyroid cells have been left in situ, the product of CaxP reaches critical values as early as one year after PTX (16).
Conclusion

In the nearest future, we will undoubtedly face a significant change in our approach to therapeutic management of secondary hyperparathyroidism in dialyzed patients. Even today, we observe a decrease in the number of patients referred for surgical treatment. This phenomenon results in part from increasingly better prophylactic measures, which do not allow for the disease to develop, as well as from early qualification of patients for kidney transplantation, but also from introduction of new pharmaceutical agents, which are an alternative for surgery. Their effectiveness will be proven in the years to come. Nevertheless, surgery performed by an experienced surgeon continues to remain a good and safe treatment modality in patients with the disease.

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