

TUMORS OF PARATHYROID GLANDS

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Parathyroid glands are small endocrine glands found in the neck which secrete parathyroid hormone or parathormone (PTH) which has a combined role together with calcitonin and vitamin D in regulating levels of calcium and phosphate concentrations in humans.

The most common disease of parathyroid glands is increased and uncontrolled secretion of PTH which is defined as primary hyperthyroidism, if it is offset as a result of intensified function of one or more parathyroid glands, or as secondary hyperparathyroidism which is mostly caused by chronic kidney insufficiency or by vitamin D deficiency.

Carcinoma of parathyroid glands is a rare disease and one of the rarest malignant endocrine tumors.

Frequency of carcinoma in patients with primary hyperparathyroidism is less than 1%.

Best treatment for patients with this primary lesion is intraoperative recognition of the tumor by surgeons, adequate resections with removal of primary lesion, and histopathological verification.

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Introduction

Malignant neoplasms – disease of modern times

Modern man lives surrounded by carcinogens because everything is contaminated, the water, the air and the food. It is established that in only one cigarette there are 30 different chemical carcinogens, and then there are many types of radiation, cesium, strontium, different types of medicaments, especially sedatives and hormones, etc. Although, nowadays we know a lot about oncogenes, we still don't have an explanation for molecular basis of carcinogenesis. It has been discovered that in the genome within the human cell, there are genes in a latent state which, when activated may cause malignant transformation, i.e. cancer.

In various stages of man's evolution and development of the society, there were frequent and lethal dangers for mankind caused by various infections and food shortages. This is explained by the fact that man was firstly a hunter and used spears, bows and arrows, until he evolved into higher forms of social organizations, concluding with present day. Along the way, tools for production were improved and socio-economic, cultural and political relations were also changed. In all of those specific stages of evolution of the society, the human environment also changed, all of the living organisms, and also various forms of human pathology were replaced by others thus giving importance to the medical science and its protective role.

It is believed that mankind could have been and actually was prone to malignant diseases from his very origin. This is confirmed by scientific research in the past decades, as well as by the numerous documents that we have inherited from ancient cultures and civilizations. Thus, cancer and malignant neoplasms are not new, unknown diseases to mankind and other living organisms. There is no doubt that better knowledge of human anatomical structure and the functions of certain organs and tissues and especially fundamental discoveries, such as microscopes and such, contributed enormously to our discovery that malignant diseases exist indeed.

Although in the beginning it was only the physicians who were interested in researching this field of work, malignant diseases, nowadays scientists from other fields of work joined in, so today it is

almost impossible to do research projects without the full involvement of physics, molecular biology, chemistry and related sciences.

Beginnings in cancer research are usually associated with an article published by an English doctor P. Pott. Namely he noticed that cancer in chimney sweepers was more frequent than in the rest of the population, probably as he himself states, because of the toxic effects of smoke and soot with which they came into contact on daily basis. At the same time, other doctors noticed that tars, lubricants and oils could be the cause of skin cancer. Some doctors have, for example, succeeded in causing cancer in various organs of animals that they were experimenting on, by treating them with petrol and tar derivatives. Later, these carcinogenic properties of tar have been confirmed by many scientists through their numerous research undertakings which involved a wider spectrum of carcinogenic substances thus a new scientific discipline called experimental oncology was formed.

Oncology, as the science of cancer, has a significant place in modern medicine, especially in prevention and protection of human health.

Endocrine oncology deals with etiology and pathogenesis, clinical pictures and tumor therapy of the endocrine system. Thanks to the application of the latest diagnostic procedures which determine the clinical endocrinology, especially neuroendocrinology and psychoneuroendocrinology, it is now possible to detect tumors of endocrine glands in time, thus enabling a significant number of patients to be cured. It is a well known fact that malignancies are constantly increasing and that they are one of the most common diseases with fatal outcome in modern times. Undoubtedly, many factors influence this enormous increase of malignant diseases. Long-term monitoring of the epidemiological study indicates that there are many carcinogenic agents. Some scientists pay special attention to the profession-related carcinogenic factors, while the majority of competent experts divide all carcinogenic substances in chemical, physical and biological categories, regardless of their etiology. It has been observed that many profession-related agents are connected to industrial professions, although the environmental influence, the way of life, nutrition, customs, habits (smoking, alcoholism, drug-addiction), previous illnesses, etc., all have a significant influence as well.

Inorganic matter has a significant etiological share in the development of malignant diseases. It was noticed that in many industrial spheres there is a higher mortality rate among workers working in plants with aluminum, asbestos, chrome, nickel, cadmium, arsenic, in various metalworking combines for iron processing, etc.

Organic matters are also of great significance when we speak of epidemiology and etiopathogenesis of primary neoplasms.

Because of the enormous dangers employees are exposed to all over the world, necessary measures, based on suggestions from scientific institutions, are undertaken in order to prevent possible health hazards.

A specific malignant potential arises from profession-related pneumoconiosis (dust).

Employees involved in the production of coal and petrol derivatives (various types of coal, coke, bitumen, tar) are probably the most vulnerable. This is also the case with employees in agriculture, mill industry, chemical industry, and paint and varnish industry. There is also danger for employees in the rubber industry, for uranium miners, and especially for the personnel exposed to x-ray radiation in laboratories for the preparation of radioisotope, in cases of damage to nuclear power plants, using of atomic weapons.

The goal

When we speak of malignant diseases in humans, it is important to be aware that we can reduce the number of sick individuals and consequently increase the number of cured ones only through knowledge. Humans have conquered many impediments and they are on a good path to discover the very essence of cancer.

Hypoparathyroidism

Hypoparathyroidism occurs as a consequence of lack of parathyroid tissue whether the cause is developmental disorder, or the tissue was destroyed by a pathological process or due to an error in removal of parathyroid glands during thyroidectomy. The most common cause of hypoparathyroidism is surgical removal of parathyroid glands, but nowadays the complications of thyroidectomy result in less than 1% of cases. One of the rarest conditions is congenital absence or aplasia of parathyroid glands.

Idiopathic hypoparathyroidism can be an inherited disease or a sporadic congenital disease and is often associated with thymic aplasia. It may occur during the first year of life, but it is usually manifested in childhood and it occurs at a higher rate in females (2:1). In some patients we can find circulating anti-parathyroid antibodies, as well as in members of their family but without a manifestation of the disease, which suggests the participation of auto-immune mechanism in the genesis of the disease. Similar antibodies can also be found on adrenal and thyroid tissue in patients with idiopathic hypoparathyroidism, although they do not show clinical signs of Addison's disease or hypoparathyroidism. It is interesting that idiotic hypoparathyroidism can sometimes be united with adrenocortical insufficiency, chronic lymphoid thyroiditis, insufficiency of islets of Langerhans and diabetes, chronic hepatitis, atrophy of gastric mucosa and pernicious anemia.

Patients with hypoparathyroidism usually manifest episodes of tetany, epilepsy, mental disorders or some other neurological signs, and there are also certain morphologic changes which can assist in giving a precise diagnosis. Patients often have epidermal lesions with rough and scaly skin, nails are deformed and fragile, hair and body hair are thin, rough and dry. There are cases of lenticular cataract

also. At the beginning of the disease, dental aplasia and hypoplasia occur on teeth which are developing, so the roots of the molars are flattened. Lamina dura thickens, and there is an occurrence of bilateral spotted calcifications in basal ganglia and cerebellum, which probably results in epileptic seizure. As a rule hypocalcemia and hypocalciuria are manifested along with hyperphosphatemia and hypophosphaturia. A disorder in mineral levels requires a substitution therapy with parathyroid hormones.

Some authors state that they have found fat tissue in place of parathyroid glands, while others state that during autopsy they did not find any parathyroid glands. There was a case of a two-and-a-half year old girl who had treatment for primary hypoparathyroidism, suprarenal gland insufficiency, hepatic cirrhosis, and was sent for autopsy because of rapid progression of lethal outcome. At the autopsy, serial intersection of both lobes and the isthmus of thyroid glands was performed but no tissue of parathyroid gland was found, neither macroscopically nor histologically (1).

Hyperparathyroidism

Hyperplasia of parathyroid glands

1. Primary hyperplasia

For a long time every nodus in parathyroid glands which was not cancer was considered to be adenoma. In 1958 the existence of primary hyperplasia within major cells of parathyroid glands was proven, and the fact that even though it affects all four glands, it may be more distinct in one or more glands, simulating adenoma in such a way. Since that time, a lot of studies have appeared which indicate the importance of primary hyperplasia of major cells as the cause of hyperparathyroidism, while, nowadays, some experts even consider that to be the most important cause of primary hyperparathyroidism. However, some other publications still show a greater frequency of adenoma. The results of 557 studies of primary hyperparathyroidism have shown that in over 80% of cases of primary hyperparathyroidism is caused by adenoma (2).

Primary hyperplasia of the major cells occurs in about 15% of patients suffering from primary hyperparathyroidism. It appears more often in the younger population, it can be present in the whole family, and in one sixth of the patients with primary hyperplasia other endocrine glands are also effected (multiple endocrine neoplasia).

The line viewed macroscopically in the earliest stage of hyperplasia shows rounding of the already flattened gland, which progressively turns into a spheroid shape. The glands can be normal size, with just a little bit of increase in size or they can increase significantly in size. A single hyperplastic gland can be only 100mg in weight while the combined weight of parathyroid glands may weigh between 1-25gm. Although all the glands are usually hyperplastic, the lower pair is usually bigger, and it is not rare to find one gland bigger than the others.

In such cases macroscopic differentiation of adenoma is very difficult. In practice every gland that weighs more than 60mg is suspected as abnormal, although the surgeon can not specify in situ a minimal enlargement along these lines. Hyperplasia is usually homogenous and diffused but in long-term cases there is a tendency towards modularity. Hyperplastic nodes are clearly limited and in time they become contoured by fibrous septa and they show a uniform cytological image, but we can also encounter nodes which are constituted of several cytological types. Big nodes can be haemorrhagic or cystic.

There is a rare syndrome where the medullar cancer of the thyroid gland and pheochromocytoma are joined. In such situations parathyroid glands change in appearance, and that change usually results in primary nodular hyperplasia. This syndrome is called multiple endocrine neoplasia type 2 or Sipple syndrome.

2. Secondary hyperplasia

The hyperplasia of parathyroid glands is almost a regular find in chronic insufficiency of kidneys with azotemia, in hyperphosphatemia, and hypocalcemia. It can also be found in patients with renal acidosis, and with disorder of metabolism of vitamin D. In all of these cases hyperplasia is physiologic and reflects an excessive production of parathormones caused by long-term hypocalcemia. A long-term hypocalcemia leads to a continuous growth of parathyroid glands.

3. Terciary hyperparathyroidism

The term hyperparathyroidism is introduced in order to explain the development of autoimmune hyperparathyroidism which occurs after a long-term secondary hyperparathyroidism. These changes occur in patients with chronic kidney diseases or in patients with intestinal malabsorption, in whom there is a development of parathyroid adenoma, and the patients become normocalcemic or hypercalcemic.

Tumors

1. Adenoma

Parathyroid adenoma is the most frequent cause of hyperparathyroidism and it is considered that it is in 80% of the cases responsible for primary hyperparathyroidism (3). We find adenoma in four out of five patients with primary hyperparathyroidism, while we encounter cancer in only 3% of cases (4). Parathyroid adenoma is practically always solitary and the finding of another tumor is very rare. Adenoma of parathyroid glands appears in a very wide range, but most frequently in the fourth decade of someone's life. It occurs much more frequently in women than in men, in relation 2.5:1 (5).

The size of adenoma varies within wide limits. They are usually small masses and their weight can be from 25mg to over 50g.

There is a correlation between parathyroid adenoma, values of the circulating parathormone and the level of hypercalcemia. It is stated that patients with changes on their bones tend to have bigger tumors, shorter duration of illness, and higher levels of calcium in the serum, while patients with renal calculosis on the average have smaller tumors, a longer history of illness and lower levels of calcium in serum. The difference between those two groups may result from the differences in how fast the tumor grows, and differences in how fast the hormones are secreted. Macroscopically parathyroid adenomas are small, soft, smooth, oval in shape, dark red tumors, usually darker in color than normal parathyroid glands. The tumors are well encompassed by a fragile capsule beside which can be found various remains of preserved compromised parathyroid tissue. Dissection of tumors shows tissues of homogenous appearance of dark orange or dark red color. There are often found cystic spaces filled with clear, yellowish or haemorrhagic fluid, as well as bleeding parts or necrosis. Bleeding may be the result of surgical trauma caused by the rupture of the fragile walls of blood vessels.

2. Carcinomas

Carcinomas of parathyroid glands may develop within normal glands, in glands with primary hyperplasia within the major cells, or, and this occurs vary rarely, within the adenoma.

Carcinoma of parathyroid glands is very rarely the cause of primary hyperparathyroidism-that is only in 4% of all cases (6).

Unlike adenoma which develops in fourth and fifth decades of someone's life carcinoma appears in a time span between adolescence and very old age. Contrary to adenoma, carcinoma appears somewhat more frequently in male population than female. Most of the parathyroid carcinoma is endocrinologically active and associated with very high-level calcium in serum and with bone changes such as osteitis fibrosa cystica. Similarly to other endocrine tumors it is believed that there is also dysfunctional carcinoma of parathyroid kind, but it is very difficult to differentiate diagnostically carcinoma of thyroid gland and thymus.

As far as diagnosing the malignancy, the only certain criteria is, as is also the case with other endocrine tumors, invasion of adjacent structures (thyroid, trachea, esophagus) and spreading of metastasis.

Carcinoma of parathyroid glands varies in size from 2-40gm.

Macroscopically it can appear to resemble adenoma, but it can also appear as solid and irregular multinodular mass. The capsule is generally well defined and thick, and wide fibrous bands intersect the tumor tissue. At intersections the tissue is whitish, brownish-grey or brown in color. Metastases are generally found in regional lymph glands, with the lungs being affected along with the liver and the bones as well.

Surgical excision of parathyroid carcinoma is very difficult and therefore recurrences are very common. A lethal outcome is usually the result of a very serious hypercalcemia.

Surgery of parathyroid glands

Indications for surgery

Materials and methods

Primary hyperparathyroidism-regardless of whether the predominant signs are hypercalcemia syndrome, bone-joints, urological, digestive or other disturbances, all the patients with primary hyperparathyroidism (HPT) who have clinical disturbances have an indication for surgical treatment, unless there are transparent contraindications against surgery (7).

Special importance is attributed to patients with hypercalcemia crisis. For such patients there is an enormous risk during surgery, including general anesthesia, because of dehydration and hypercalcemia, so it is important that the patients undertake a number of conservative preparations before surgery such as infusion of physiologic solution, diuretics, and administration of phosphates. In cases of renal insufficiency, dialysis should be used as part of preparation for surgery, or possibly peritoneal dialysis.

One hundred and forty-seven patients from such a group were monitored and 20% of them were operated because their diseases progressed. Recent findings have affirmed that there is a risk of so called asymptomatic HPT (8).

Thirty-four percentage of patients who were monitored at least five years have developed very serious complications (ulcus, kidney insufficiency, hypercalcemia crisis) which were the cause of lethal outcome in four patients (9). That is why nowadays it is considered that the patient with asymptomatic HPT should undergo surgery, because the danger of further evolution of the disease is much greater than morbidity and mortality of cervical exploration.

Patients with normocalcemia primary HPT who have relapses of urinary lithiasis are also candidates for cervical exploration, but only after a very careful investigation which, if required, should be repeated many times.

Secondary and tertiary HPT – patients from this group are rarely considered for surgery, only if pharmacological treatment is ineffective. They often have changes in the bones, deposition of calcium in soft tissue, or unbearable pruritus.

Surgical strategy

There are several key elements which are responsible for successful surgery of HPT. They imply that the surgeon:

Must have enough experience so that he can, without great difficulty, find all four parathyroid glands during the operation. If one or more of them are missing, the surgeon must know where the most frequent aberrant locations are.

He should be able to differentiate between normal and pathologic parathyroid, and be sure to check his impression by intraoperative histological analysis (biopsy "ex tempore").

He must stand by the principle that the essence of surgical intervention is removal of diseased and saving of healthy parathyroid glands. The extent of resection is planned around the nature of pathologic changes, because the primary operation is the best opportunity for the cause of HPT to be definitely eliminated.

In most cases, viewed macroscopically, an experienced surgeon knows how to recognize the diseased gland-hyperplastic parathyroid is, as a rule, bigger, oval or round, hyperemic and dark red in color. Adenoma are usually solitary, dark in color, ranging from a few millimeters to a few centimeters in diameter, while at the same time the other glands are suppressed, paler, flattened and soft. Carcinoma is bigger in size, hard and adherent, and if there are at the same time metastasis in the regional lymphatic glands then intraoperative identification is not hard. In an early stage and when there is no infiltration of the surrounding organs, it is hard to differentiate carcinoma from adenoma of parathyroid, and even sometimes it is hard to differentiate adenoma from hyperplastic glands.

Numerous processes have been suggested in order to help differentiation of healthy from diseased parathyroid. Intravital imaging through infusion of toluidine blue was abandoned because of the toxic effects, while the methylene blue which mostly results in coloring the changed parathyroid glands is rarely used in practice.

Another, a newer test which is more widely used is the test of density (specific weight). The test is based on the fact that cells of a normal parathyroid gland contain much more intracellular fat than in the cases of hyperplasia or tumor, so thanks to that in solutions of mannitol of certain density (1.049-1.069) pathologically changed glands sink, and the healthy ones float on the surface. This test can be used for differentiation between adenoma and hyperplasia (10).

Nowadays the surgeons mostly rely on intraoperative histological analysis, which requires a well

trained pathologist in this specific field of work. However, we must keep in mind that a competent pathologist has limited possibilities in diagnosing of adenoma, carcinoma and hyperplasia when using frozen cutouts. The surgeon expects reliable information whether a healthy or a pathologically changed parathyroid gland is in question, and that kind of conclusion is safest if it is based on the content of intracellular fats (11).

Technical principals – the surgeon should be relaxed and concentrated on this operation, without making plans for any other activities, and it should always be scheduled the first thing in the morning.

The patient should be well-situated on the operating table with the neck in hyperextended position. A low collar incision from one outer edge to the other outer edge of m. sternocleidomastoideus should provide fairly wide access. Meticulous hemostasis is applied in order to enable recognition of fine anatomic structures, such as parathyroid glands and n. recurrens, which is difficult and impossible when bleeding occurs. During the operation the patient should not lose more than a few cubic centimeters of blood.

In order to discover the parathyroid glands, a lobe of the thyroid gland should be freed and mobilized in front and inside, which will enable access into tracheoesophagus space. A. thyroidea inferior and n. recurrens must be found; as the basic anatomic marks they help us discover the position of parathyroid glands. Biopsy of the parathyroid gland should be cautiously executed on the antihilar side so that there is no damage of vascularization. If a. thyroidea superior is missing you should look for it in retropharyngeal, tracheoesophageal sulcus and retroesophageal space as well as intrathyroidally. If a. thyroidea inferior is not present in the expected space you should execute thymectomy through the existing cervical access (12).

Volume of resection-the volume of resection depends on the cause of the disease. The most common cause is adenoma, sometimes hyperplasia, and exceptionally rarely carcinoma (13).

Table 1. The causes of primary HPT (26)

Author	Number of operated	Adenoma	Hyperplasia	Carcinoma
Russell	500	79%	15%	0.4%
Cady	104	87.5%	11.5%	1%
Headman	839	87%	12.8%	0.2%

Table 2. Number of enlarged parathyroid glands in a 100 patients with primary HPT (27)

Number of enlarged glands	Number of patients
1	65
2	15
3	10
4	10

It is logical that the volume of resection is planned in a way that allows us to remove the diseased glands and save the healthy ones. When only one gland is contaminated, as is characteristic for adenoma, it is extirpated. The remaining glands in uniglandular form of disease macroscopically appear normal, or they are atrophic, so in that case it is enough to do biopsy on one of them so that the pathologist can intraoperatively confirm its normal structure.

In cases of parathyroid carcinoma the tumor is removed together with an appropriate thyroid lobe, accompanied by regional dissection of lymphatic nodes. It is important that in the course of preparation the tumor capsule is not opened, because the tumor cells are capable of local implantation which can lead to relapse (14). It is also best to surgically remove the distant metastasis if they are approach-able because they are hormonally active. These patients are directly threatened by hypercalcemia and the possibility of pharmacological treatment is very limited.

It is undoubtedly the hardest task to choose the right type of operation for patients with hyperplasia of all four parathyroid glands, whether we are talking about hyperplasia of major cells or bright cells. By executing the classical subtotal 31/2 parathyroidectomy we leave 40-60mg of well vascularized tissue in situ, and we can achieve normocalcemia in majority of patients, but relapses are not rare. Permanent hypoparathyroidism also appears. In order to reduce the risk of hypoparathyroidism in cases of subtotal parathyroidectomy to a minimum, it is necessary that after the identification of all four glands and histological verification first of all we recess the part of the gland which is intended to remain. Only when we are sure that its vitality has been preserved we can perform extirpation of the rest. If the removed tissue is subjected to deep freezing it can be saved 9 to 12 months and if the need arises it can be used for autotransplantation (15).

An alternative cure for hyperplasia of all parathyroid glands is total parathyroidectomy and autotransplantation 40-60 mg in the muscle. This method is particularly recommended when the whole of the family is effected and in cases of secondary hyperparathyroidism.

The technique in transplantation of parathyroid tissue-the technique used in transplantation is not complicated. Removed parathyroid gland is im-

mediately after extirpation placed in freezing physiologic solution or in the solution for tissue culture. In the freezing physiologic solution, apart from the fact that the metabolism slows down to a minimum, the gland also achieves the necessary firmness, so that it can be easily cut into fragments of 1x1x2mm in diameter. After being previously histologically confirmed that it is parathyroid tissue indeed, every fragment is transplanted into the muscle tissue, in a special pouch formed by blunt separation of muscle fibers. At the same time bleeding within the muscle must not occur. In the beginning the transplant is nourished by diffusion and it takes several weeks for it to start functioning. The most common places for transplantation are m. sternocleidomastoideus in the neck region, and the brachioradialis muscle of the forearm of non-dominant arm. If no rough technical omissions occur, the transplant definitely becomes accepted. Up till now, many statements about relapses of HPT caused by hyperplasia in the transplant have been published. In such cases surgical excision is performed in local anesthesia because of the transplanted tissue (16).

Results

Effects of primary operations and the results of treatment

According to data from famous institutions worldwide which are specialized in dealing with this problem, in primary operation the surgeon is capable of finding the cause of hypercalcemia and correcting it successfully in 85-95% of patients with primary HPT (17).

By doing extirpation of the diseased parathyroid tissue, normalization of calcium in plasma is achieved very quickly. After a successful operation relapse may occur. Unlike in cases of persisting hypercalcemia, only cases in which the patient has been without hypercalcemia at least six months after the primary operation are marked as relapses.

Definitely the optimum results of surgical treatment of primary HPT are achieved in parathyroid adenoma. Extirpation of adenoma which has developed in only one parathyroid gland has registered definite healing in over 99% of patients (18).

Out of 3204 patients in whom the disease was caused by only one gland, relapse occurred in 24 patients (0.7%) at a later stage (19).

With parathyroid carcinoma relapse is quite common, although parathyroid carcinoma is very rare.

Reoperation

The need for reoperation occurs when in the primary operation the cause (persisting HPT) is not found and eliminated or because of relapse.

The major characteristic of reoperation is that it is performed in the scar and in altered anatomic relations. The possibility of finding parathyroid glands in repeated surgery is lesser than in primary operation, including more risks and complications caused by surgery.

After reoperation, hypercalcemia persisted in about 21% of patients, in 24% of them permanent hypoparathyroidism was developed, in one case a permanent tracheotomy was done because of bilateral recurrent nerve lesions, while 2 out of 35 of operated patients died because of intraoperative lesions of the larger blood vessels in the neck (20). Stated data illustrates how exceptionally delicate reoperations on parathyroid glands are, and demands caution when deciding on surgery, in the sense that: HPT diagnosis should be reviewed again. To patients with mild forms of disease and light hypercalcemia surgery is usually not recommended, only occasional thorough check-ups.

For patients where surgery is necessary one must do a detailed study of operative findings from the previous surgery and re-check pathohistological slides.

Reoperation is based on the same principles of operative techniques as the primary operation. Cervical approach is used with excision of the scar as opposed to the previous incision.

The side, on which the cause of the disease is probably to be found, is the side that is always firstly explored. When there are significant changes on the scar, exploration is usually done through the space between carotid space and thyroid glands. During surgery in over 50% of the cases parathyroid adenoma is found in the place which corresponds to the normal anatomic location (21). In these cases the localization of the diseased gland is subnormal or ectopic and is usually found in anterior or posterior mediastinum, intrathyroidally or in the carotid membrane. After a detailed exploration of the neck and transcervical thymectomy is done, and the cause of HPT not is found, we can begin with exploring mediastinum through longitudinal sternotomy. Sometimes reoperation begins with mediastinotomy, primarily if all four parathyroid glands in the neck were identified in the previous surgery, or if by using topographic diagnosis the presence of adenoma in the mediastinum was proven. Longitudinal sternotomy is used in about 20% of patients who undergo reoperation, although that percentage could be reduced (22). Namely, for some adenoma localized in the front mediastinum and extirpated through sternoto-

my, only when the tumor is found it becomes clear that it was available for extirpation by transcervical access (23).

Most of the ectopically localized adenoma in the frontal mediastinum is in close anatomic relation with thymus, so thymectomy is usually an integral part of mediastinum exploration. Adenoma localized in the posterior mediastinum can, by rule, be removed through the neck. If the cause cannot be found either in the neck or in the mediastinum, resection of one or both of thyroid lobes is considered because of possible intrathyroidal location.

The success of reoperation in treating primary hyperparathyroidism of HPT is rather smaller than the success in primary operations.

Hypercalcemia is corrected in 63-91% (24).

Hypercalcemia remains in 9-27% of patients who are reoperated, and it requires new exploration with higher risk of complications, or the disease progresses further and usually ends up with renal insufficiency.

Second significant deficiency of reoperative therapy of HPT is permanent hypoparathyroidism, which is registered in highly specialized institutions in 3-24% (25).

Chances that the patient may lose the parathyroid gland after reoperation are increased for two main reasons. First of all in primary surgery often normal parathyroid glands are removed as well but the adenoma which was not detected remains, and secondly because during reoperation there is a higher level of devascularization and traumatic damage of normal parathyroid tissue.

This problem is nowadays successfully overcome by the possibility of using direct autotransplantation and preservation of part of the parathyroid tissue by deep-freezing it, which can, at a later stage if necessary, be used for transplantation.

Discussion

Carcinoma of parathyroid glands is very rare, and in the structure of all malignant tumor diseases it shows in only 0.003%.

Clinical picture of carcinoma in parathyroid glands is very variable and depends on the fact if the tumor is functional or non-functional.

Surgical complications range from n. recurrens to hypoparathyroidism.

Conclusion

Because it is not very common, carcinoma of parathyroid glands is an insufficiently researched malignant tumor for whose treatment there are no clear instructions. Surgery remains the major form of treatment.

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TUMORI PARATIROIDNIH ŽLEZDA

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Paratiroidne žlezde su male endokrine žlezde u vratu čoveka koje sekretuju paratiroidni hormon ili parathormon (PTH), koji zajedno sa kalcitoninom i D-vitaminom ima primarnu ulogu u regulaciji koncentracije kalcijuma i fosfata u organizmu.

Najčešće oboljenje paratiroidnih žlezda predstavlja povećano i nekontrolisano lučenje PTH koje se može definisati kao primarni hiperparatiroidizam, ako nastaje kao posledica pojačane funkcije jedne ili više paratiroidnih žlezdi ili kao sekundarni hiperparatiroidizam koji se javlja najviše u hroničnoj bubrežnoj insuficijenciji ili kao posledica deficita vitamina D.

Karcinom paratiroidnih žlezdi je veoma retko oboljenje i predstavlja najređi maligni endokrini tumor.

Učestalost karcinoma kod bolesnika sa primarnim hiperparatiroidizmom je manja od 1%.

Intraoperativno preoznavanje ovog tumora od strane hirurga i adekvatna resekcija sa odstranjivanjem primarne lezije, uz patohistološku verifikaciju su najbolji tretman za bolesnike sa ovom primarnom lezijom.

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Ključne reči: paratiroidne žlezde, neoplazme, hirurgija, operativne procedure, hiperparatiroidizam

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