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Parathyromatosis as a cause of recurrence primary hyperparathyroidism: A case report

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ABSTRACT

INTRODUCTION AND IMPORTANCE: Parathyromatosis is a rare cause of recurrent hyperparathyroidism. The main cause of this pathology is secondary implantation into the surrounding tissues of the damaged parathyroid gland (rough manipulation of the gland tissue) during the primary operation. Nowadays, parathyromatosis remain a difficult diagnostic and therapeutic task.
CASE PRESENTATION: A 57-year-old woman 12 years ago underwent right inferior parathyroid adenomectomy. For the last 2 years, the patient began to worry about pain in large tubular bones, thoracic spine. In the biochemical analysis of the patient's blood, the serum ionized calcium level was increased - 1.56 mmol/l, parathyroid hormone - 144 pg/ml. Ultrasound scan of the neck showed the presence of two hypoechoic formations with dimensions of 24 × 12 × 6 mm and 14 × 9 × 8 mm behind the right lobe of the thyroid gland (the site of a previously operation).The patient underwent cervicotomy, removal of 3 fragments of the parathyromatosis tissue. According to a histological study, there fragments are presented by diffuse-nodular hyperplasia from dark main cells. Remission of primary hyperparathyroidism was achieved.
CLINICAL DISCUSSION: This clinical case shows the need for differential diagnosis in recurrence primary hyperparathyroidism with parathyroid cancer, secondary hyperparathyroidism, parathyromatosis.
CONCLUSION: The main method of treatment is the surgical removal of all foci of parathyromatosis. In the postoperative period, observation of such patients is required with laboratory and visual screening to exclude recurrence hyperparathyroidism.

1. Introduction and importance

The generally accepted method of treating primary hyperparathyroidism (HPT) is the selective removal of parathyroid adenoma (parathyroid adenomectomy) [1]. To improve the effectiveness of the results of surgical treatment, It's uses an integrated approach to preoperative imaging and intraoperative monitoring of the dynamics of intact parathyroid hormone (iPTH) [1]. Despite this, 2–9% of patients who underwent primary parathyroid adenomectomy develop persistence or relapse of hyperparathyroidism [2,3]. The main reasons include: the presence of an atypically located parathyroid gland and/or undiagnosed multiglandular disease [3]. Parathyromatosis is a rare cause of recurrent hyperparathyroidism [4]. Its morphological basis is multiple foci of hyperactive parathyroid tissue, which are scattered in the soft tissues of the neck and/or mediastinum [5]. The main cause of this pathology is secondary implantation into the surrounding tissues of the damaged parathyroid gland (rough manipulation of the gland tissue) during the primary operation [4,5]. Most often occurs in patients who have undergone surgery for familial primary or secondary renal hyperparathyroidism [4–6]. Parathyromatosis is extremely rare in primary sporadic hyperparathyroidism [4].

We present our experience of successful diagnosis and surgical treatment of parathyromatosis in a patient with primary sporadic hyperparathyroidism. This case report has been reported in accordance with the SCARE Criteria [7].

2. Case presentation

A 57-year-old pensioner Eurasian woman 12 years ago underwent right inferior parathyroid adenomectomy (histological confirmed) without using intraoperative iPTH monitoring. In the postoperative period, the patient has not been under the care of endocrinologist. The patient has not been using drug, and also she denied the presence of family and hereditary diseases. She had not any other past surgical history and chronic diseases. For the last 2 years, the patient began to worry about pain in large tubular bones,

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thoracic spine, and weakness. In the end, she was examined by an endocrinologist at the place of residence a year after the appearance of these complaints - a relapse of hyperparathyroidism was revealed. She was referred to an endocrine surgeon in our clinic.

In the biochemical analysis of the patient's blood, the serum total calcium level was increased - 2.77 mmol/l (reference values 2.1–2.6 mmol/l), ionized calcium - 1.56 mmol/l (reference values 1.15–1.27 mmol/l), parathyroid hormone - 144 pg/ml (reference values 15.0 - 68.3 pg/ml), vitamin D - 21 ng/ml (reference values> 30 ng/ml), creatinine - 74 μmol/l (reference values 50–120 μmol/l). The daily urinary excretion of calcium was 2154 mmol/day (reference values 2.5–6.25 mmol/day). The estimated level of glomerular filtration rate according to the CKD-EPI formula (2011) is 78 mL/min/1.73 m2.

An ultrasonography (US) scan showed the presence of two hypoechoic formations with dimensions of 24 × 12 × 6 mm and 14 × 9 × 8 mm behind the right lobe of the thyroid gland in the region of its middle third. There was not any mass that could be identified as a parathyroid adenoma or parathyroid hyperplasia. The total volume of the thyroid gland was 14.5 cm^3, the right lobe was 11.0 cm^3, the left lobe was 3.5 cm^3. Regional lymph nodes 4–5 mm in size; cystic changes, hyperechoic inclusions are absent. A scintigraphy scan did not show an increase in the functional activity of the parathyroid glands. Bone mineral density scan showed that the minimum T-score was -2.6 in the left forearm.

According to the preoperative study, surgical intervention was planned in the amount of cervicotomy, revision of the right neck, right upper parathyroid adenomectomy with intraoperative monitoring of iPTH.

The operation took place on November 18, 2020. The operation was performed by an endocrine surgeon who has 16 years of experience in this area. A cervicotomy was performed according to a standard technique. There was a pronounced cicatricial process in the area of the middle third of the right lobe of the thyroid gland (the site of a previously right inferior parathyroid adenomectomy in 2008). In this zone, there were 3 fragments of an ovoid shape, located in the central tissue of the neck, ranging in size from 5 to 10 mm, dark brown, without a capsule. All fragments were located ventrally in relation to the right recurrent laryngeal nerve (RLN). The right upper parathyroid gland was located in the region of the upper third of the right lobe of the thyroid gland, dorsally to the right RLN, 3 × 6 mm in size, brown, not visually changed. The mobilization and removal of the described 3 fragments of the parathyroid tissue were performed. The operation was supplemented by taking a biopsy of ¼ of the tissue of the right upper thyroid gland, a fragment of the right lobe of the thyroid gland, and pretracheal tissue with a lymph node in the operation area. Dynamics of the level of intraoperative monitoring of iPTH: before the skin incision - 209 pg/ml; at the time of mobilization of 3 fragments of parathyroid tissue - 120 pg/ml; 10 min after the removal of these fragments - 17.5 pg/ml. Intraoperative test according to Miami criterion – positive [8].

According to the histological study, 3 removed fragments of parathyroid tissue are represented by diffuse-nodular hyperplasia from dark main cells. These fragments do not have their own capsule and area of unaltered parathyroid tissue along the periphery. In addition, there was no trabecular growth, vascular invasion (Fig. 1).

On sections of a biopsy ¼ of the right upper parathyroid gland, there was normal parathyroid tissue. A tissue fragment of the right lobe of the thyroid gland is represented by a normofolicular type of structure without invasion of the parathyroid tissue. The pretracheal tissue is represented by adipose tissue, and the lymph node had a normal structure also without invasion of the parathyroid tissue.

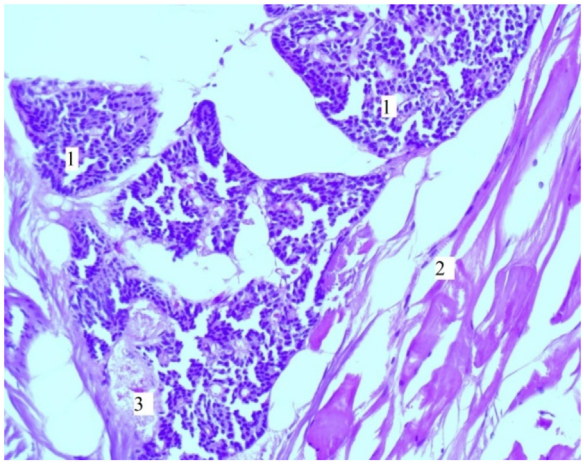

Fig. 1. Microphotography of operative material. Tinted with hematoxylin and eosine. Magnification 20x0,40. **The tissue of the focus of parathyromatosis**. 1 - areas of diffuse-nodular hyperplasia from the dark main cells of the parathyroid gland; 2 - scar connective tissue; 3 - a blood vessel without signs of invasion of the main cells into its wall.

In the postoperative period, laryngoscopy was performed, on which the normal mobility of the vocal folds was established. On the first day after surgery, the level of iPTH was 116 pg/ml, the level of serum total calcium was 235 mmol/l, the ionized calcium level was 1.20 mmol/l. She was discharged in a satisfactory condition on the 7th day after the operation. The patient was examined 2 months after the surgery: no active complaints; the level of total blood calcium is 2.16 mmol/l. In the patient's opinion, the treatment carried out helped her.

3. Clinical discussion

Parathyromatosis is a rare cause of recurrence of primary sporadic HPT. In literature, 21 such cases are described [4]. According to our information search using the keywords primary hyperparathyroidismänd parathyromatosisin the Russian-language database Elibrary: no similar observations were found.

Three theories of the development of parathyromatosis have been proposed: low-grade parathyroid tumor; secondary implantation into the surrounding tissues of the damaged parathyroid gland (rough manipulation of the gland tissue) during the primary operation; transformation of additional parathyroid nodules remaining in the process of embryogenesis [5]. The main contingent is patients with secondary hyperparathyroidism in chronic kidney disease, since after parathyroidectomy, a set of pathogenetic factors remains, which lead to the progression of structural changes in the parathyroid glands/tissue [5,6]. The most frequent localization of the foci of parathyromatosis is the place of the thyroid gland and places of autotransplantation of the parathyroid glands, such as the forearm or sternocleidomastoid muscle [4,5]. In addition, foci of parathyromatosis in adipose tissue adjacent to the recurrent laryngeal nerve, retrosternal region, fascial sheath of the main neurovascular bundle of the neck, thymus, upper mediastinum and tracheoesophageal sulcus have been described [9].

Diagnosis of parathyromatosis is a difficult task, both at the preoperative stage of the examination and during surgery. Parathyroid cancer is the main disease that must be excluded in the differential diagnosis of parathyromatosis based on clinical, laboratory, visual and morphological data [5]. Patients with parathyroid cancer usually have more severe hypercalcemia and metastatic disease [5,10]. Options for preoperative diagnostics were considered: foci of parathyromatosis can be detected on ultrasound, scintigraphy and multispiral computed tomography. Small lesions fused with

surrounding tissues may not be visible on ultrasound and scintigraphy [9]. According to the imaging methods and the intraoperative examination, parathyromatosis is characterized by the presence of small and multiple foci of glandular tissue, while cancer is a solid tumor. In addition, the foci of parathyromatosis are often surrounded by fibrous tissue as a manifestation of the scar process after previous surgery, which can give the impression of cancer [10]. Therefore, some authors recommend a radical approach to surgical treatment as if their lesions were malignant, because latent tumors can be present in both conditions [11]. Histopathological criteria for parathyroid cancer include: trabecular growth pattern, thick fibrous capsule, number of mitoses> 1/10 per field of view, capsular invasion, vascular invasion, lymph node metastases or distant metastases [10]. Unlike adenomas and cancers of the PTG, the foci of parathyromatosis lack their own capsule. The main treatment for parathyromatosis is the surgical removal of all lesions [5]. The effectiveness of the operation performed for parathyromatosis is considered doubtful due to the complexity of intraoperative detection of all foci that are not observed in the preoperative localization. Moreover, several surgeries may be required to achieve complete remission [11].

In the presented clinical observation, we were faced with a difficult diagnostic task. Firstly, 12 years ago the patient underwent right inferior parathyroid adenomectomy. We are not aware of the nature of manipulation of the adenoma and the technique of the operation, which did not exclude the possibility of contamination of nearby tissues with remnants of the adenoma. Secondly, the secondary nature of hyperparathyroidism was not excluded. The patient's renal function was normal, there was a vitamin D deficiency, for which the patient received a maintenance dose of cholecalciferol. Thirdly, there was the possibility of undiagnosed multiglandular disease or parathyroid cancer.

Normal renal function and the absence of multiple lesions according to imaging methods excluded the possibility of multiple lesions, both primary (multiglandular disease) and secondary (secondary HPT in chronic kidney disease or chronic vitamin D deficiency). The situation is assessed ambiguously, since the picture of the disease could correspond to both the foci of p parathyromatosis and the adenoma of the upper right PTG.

According intraoperative examination, it was found that the upper right thyroid gland was intact (confirmed by biopsy), and the lesions were located directly in the area of the previously performed surgical intervention. Since the regional lymph nodes were not enlarged, there was no growth of foci in the nearby tissues and in the right lobe of the thyroid gland, the proposal for parathyroid cancer was also rejected. The results of histological examination showed that the removed foci are represented by hyperplastic tissue without signs of malignancy, without invasion into the right lobe of the thyroid gland and regional lymph nodes, which fits into the diagnosis of parathyromatosis. The performed operation made it possible to remove all existing foci of parathyromatosis, and the positive dynamics of intraoperative iPTH monitoring confirms its radicality.

4. Conclusion

Parathyromatosis is a rare cause of recurrence primary hyperparathyroidism. The basis of relapse in this situation is gross manipulation of the tissue of the parathyroid adenoma with destruction of the capsule of the latter, which leads to the contamination of nearby tissues with cells of the adenoma. The main method of treatment is the surgical removal of all foci of parathyromatosis. In the postoperative period, observation of such patients is required with laboratory and visual screening to exclude recurrence hyperparathyroidism.

Conflicts of interest

No conflicts of interest regarding this publication.

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Ethical approval

This case report is exempt from ethical approval at our institution as this is not a research study.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Ilyicheva E.A. – the surgical stage of therapy; data analysis and interpretation; development of the concept and design; substantiation of the manuscript and verification of critical intellectual content; editing and final approval of the manuscript.

Bersenev G.A. – development of the concept and design; collection of material, analysis and interpretation of data, substantiation of the manuscript and verification of critical intellectual content.

Registration of research studies

Not applicable.

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