

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Video-assisted thoracoscopic surgery for primary hyperparathyroidism with ectopic parathyroid adenoma in thymus

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SUMMARY

Introduction Primary hyperparathyroidism is rare pathology in children (2–5:100,000). In more than 85% of patients, a single adenoma is present, and its extirpation is usually the only treatment a patient requires. In approximately 15–80% of cases, ectopic mediastinal parathyroid tissue can be found inside the thymus.

Case outline Our patient was a 13-year-old boy, who presented with multiple bone fractures in the previous period of time, and fatigue. Parathyroid hormone levels preoperatively were extremely high (1320 pg/ml – more than 19 times higher than normal). Serum calcium was also elevated (total 3.55 mmol/l; ionized 1.41 mmol/l). He was examined and diagnosed as primary hyperparathyroidism by a pediatric endocrinologist. Imaging procedures for the preoperative localization of parathyroid adenomas were done (^{99m}Tc sestamibi scintigraphy and magnetic resonance imaging suggested ectopic mediastinal parathyroid adenoma). The patient underwent video-assisted thoracoscopic surgery procedure. After exploration of the mediastinum and chest, no ectopic parathyroid tissue was found, so total thoracoscopic thymectomy was performed. Final pathological section confirmed parathyroid adenoma inside the thymus.

Conclusion We believe that if no parathyroid tissue is found during surgical exploration of mediastinum, in a child with preoperatively detected parathyroid adenoma in anterior mediastinum, recommendation is to think about possible intrathymic localization and consider removing the thymus. Greater sample size is necessary for higher reliability of this statement.

Keywords: primary hyperparathyroidism; video-assisted thoracoscopy; thymectomy; Tc-99m sestamibi parathyroid scan; children

INTRODUCTION

Primary hyperparathyroidism (PHPT) is rare in pediatric patients (2–5:100,000) and only about 200 cases have been reported [1]. Clinical presentation can include unspecific symptoms of gastrointestinal, musculoskeletal, renal, and neurological systems, but also very specific such as pathological bone fractures, kidney stones, or pancreatitis [2]. It is usually diagnosed by an endocrinologist, however appropriate treatment for insufficiently controlled PHPT is mainly surgical. PHPT is principally caused either by adenoma or hyperplasia of parathyroid glands. In more than 80% of patients, a single adenoma is present, and its extirpation is usually the only treatment a patient needs [3, 4, 5]. Preoperatively, it is necessary to detect hypersecreting gland(s) or to locate adenoma. This can be achieved using ultrasound, magnetic resonance imaging (MRI), computerized tomography (CT) or radioisotope scan. Also, intraoperative monitoring of parathyroid hormone (PTH) levels, frozen section biopsy, handheld gamma probe or methylene

blue infusions should be used as a direct control of the adequate extirpation [6]. The goal of the surgical treatment is to identify and remove all abnormal parathyroid tissue.

The purpose of the study was to present our first experience in such a rare pathology, and to consider treatment options when pre- and/or intra-operative mass detection is inconclusive.

CASE REPORT

Our patient was a 13-year-old boy, who presented with multiple bone fractures in the previous period and fatigue. He was examined and diagnosed as PHPT by a pediatric endocrinologist. PTH levels were extremely high (1320 pg/ml – more than 19 times higher than normal). Serum calcium was also elevated (total 3.55 mmol/l; ionized 1.41 mmol/l), serum phosphorus was low (0.45 mg/dl), alkaline phosphatase was normal, 25-hydroxyvitamin D (25OHD) was low (29 nmol/l) and biochemical markers of bone turnover were also high (CrossLaps 2895 pg/ml

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Figure 1. Preoperative diagnostics – ^{99m}Tc -sestamibi scan showed intensive focal uptake in mediastinum

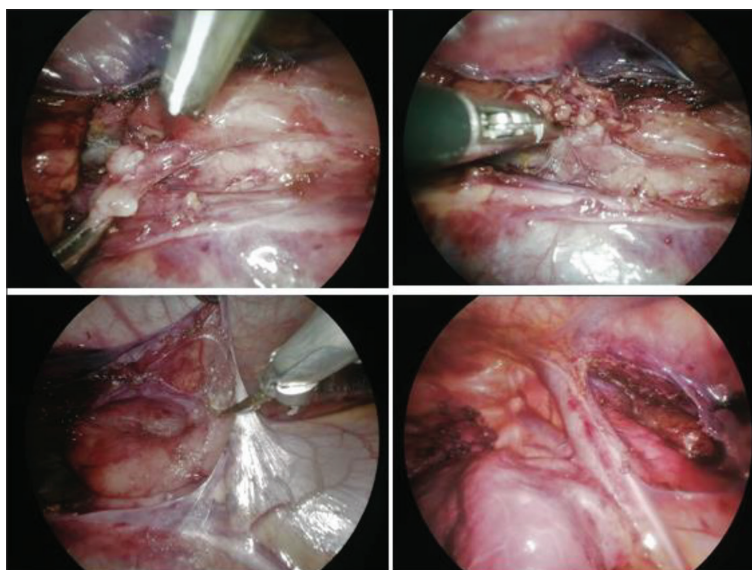


Figure 2. Intraoperative details – suspicious mass (without parathyroid tissue) extirpation (upper row) as well as initial and final step of thoracoscopic thymectomy (lower row)

and P1NP > 1200 ng/ml). Urinary excretion of calcium was high with urinary calcium/creatinine ratio of 2.1. We did biochemical screening for hyperparathyroidism and the other multiple endocrine neoplasia type 1 (MEN1) -related tumors, and it was negative.

Standard X-ray images of target bones were taken (distal part of the left humerus with reduced bone density, in its proximal and middle parts were seen pseudocystic resorption zones, similar changes in distal part the right humerus and proximal right radius and ulna, reduced bone density of both femurs and right tibia).

Ultrasound of the neck was unspecific. Neck CT marked suspicious hyperplastic parathyroid tissue (5 mm) in the inferior aspect of the left thyroid lobe. Chest MRI showed some suspicious masses in close relation to both brachiocephalic trunks, which had characteristics of ectopic parathyroid tissue, lymphatic or fatty tissue.

^{99m}Tc -sestamibi scintigraphy including single-photon emission computed tomography study of the neck and mediastinum showed focal intensive uptake in the anterior part of the right mediastinum, which refers as ectopic adenoma or parathyroid gland hyperplasia (Figure 1).

Initially, the patient was treated conservatively with saline rehydration and diuretics, once with bisphosphonates infusion, and vitamin D supplements. Calcium level was normalized preoperatively.

After consultations with endocrinologists, adult general surgeons, otolaryngologist, adult thoracic surgeon and pediatric cardiothoracic surgeon, minimally invasive surgery was planned. The original plan included preoperative low dose methylene blue infusion, which should have accumulated into the ectopic parathyroid tissue and stained it blue. Unfortunately, intravenous methylene blue solution in our country was not available. Our decision was to perform surgery without intraoperative adenoma marking on. Intraoperative PTH levels monitoring and

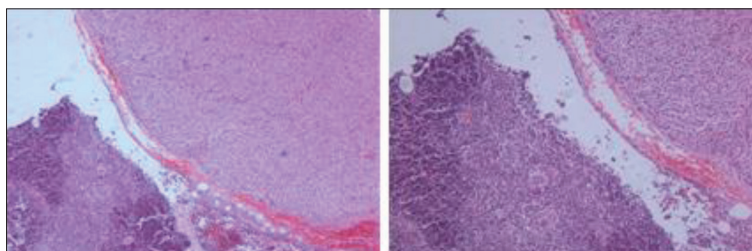


Figure 3. Final pathological section (50× and 100× magnified) – the nodule consisted of regular-looking parathyroid tissue surrounded by regular thymic tissue

intraoperative localization with hand-held gamma counter probe were technically impossible as well. At last, frozen section biopsy was planned as intraoperative confirmation of parathyroid tissue removal.

Video-assisted thoracoscopy was performed under general anesthesia with supine positioned patient. Camera port of 5 mm was located in the fifth right intercostal space in the midaxillary line. Two working 5 mm ports were placed into the fourth and sixth right intercostal space in the anterior axillary line. A single suspicious mass was extirpated, but frozen section confirmed presence of regular thymus parenchyma and reactive lymph node inside the fatty tissue, without parathyroid tissue. Total thoracoscopic thymectomy was performed (Figure 2). Resected thymus had dimensions $10 \times 4 \times 3$ cm and weighed 34.4 g. The capsule was thin and smooth. On cut surface, the regular thymic tissue was grayish to whitish, elastic, soft, lobular. In the upper pole of the right lobe, there was a well-circumscribed and encapsulated whitish nodule measured 11×4 mm. After removing the thymus, detailed exploration was repeated, and again no suspicious ectopic parathyroid tissue was found. Chest tube was placed, and lung re-expanded. There were no intraoperative complications and neat hemostasis was achieved.

Blood samples were collected at the beginning of the surgery, 10 minutes after removing the thymus, as well as 12 and 24 hours postoperatively. These results, which we could not get until the next day, showed that PTH levels

decreased down to normal (35.6 pg/ml after 10 minutes and 33.1 pg/ml after 12 hours), as well as calcium levels.

Final pathological section confirmed ectopic parathyroid adenoma, surrounded by regular thymic tissue (Figure 3).

We confirm that we have read the journal's position on issues involving ethical publication and affirm that this work is consistent with those guidelines.

Considering that our patient was a minor, all the data was published after obtaining parental consent.

DISCUSSION

PHPT has bimodal distribution in pediatric population. In newborns, this genetic condition is usually presented with all four glands hyperplasia. Another peak is in older children and adolescents, and is usually caused by single parathyroid adenoma (80%) [3–6]. Parathyroid carcinoma is extremely rare cause in children [7].

In approximately 15–80% of cases, ectopic mediastinal parathyroid tissue can be found inside the thymus [6, 8–12]. Inferior parathyroid glands and thymus both originate from the third pharyngeal arch [3, 6, 13]. Other common localizations of ectopic parathyroid tissue include mediastinum, thyroid gland, and parapharyngeal space [3, 9, 14–17]. Signs and symptoms of hyperparathyroidism can also be the first presentation of MEN1. This syndrome, beside parathyroid adenoma, includes intestinal-pancreatic endocrine tumors and pituitary tumors [13].

There are still no specific guidelines for precise preoperative localization of parathyroid tissue. Preoperative neck ultrasound facilitates spotting suspicious homogenous echoic nodule. This diagnostic tool is unable to detect mass which is not superficial, neither a mass which is behind air-filled structures. Also, masses that are located behind the sternum or generally in the mediastinum are not accessible. CT is not commonly used in children. MRI is a safe and non-invasive diagnostic imaging modality which can be used to detect suspicious ectopic nodules inside the mediastinum. Its disadvantages include poor differentiation between parathyroid tissue and lymph nodes [1]. The method of choice for localization of ectopic parathyroid tissue is parathyroid scintigraphy [18].

In our case, results of used diagnostic tools were quite different. However, MRI and radioisotope scan both spotted suspicious ectopic parathyroid tissue inside the mediastinum, with slight difference in its precise localization.

Bilateral four-gland neck exploration was the most commonly used surgical technique for treating hyperparathyroidism [16]. Unilateral neck exploration is considered appropriate in asymptomatic patients with mild forms of PHPT [16, 19].

Open cervical approach (collar incision by Kocher) can also be used for mediastinal adenomas located in close relation to the aortic arch, or more cranially located masses [3, 16].

For masses located deeper inside the mediastinum, instead of standard open techniques such as thoracotomy, median sternotomy and manubriotomy, minimally invasive approaches are developed as well (video-assisted

mediastinal surgery [13, 17] and video-assisted thoracoscopy [20–23]. It is considered a “first line” treatment option for patients with mediastinal parathyroid adenoma located deeper than the brachiocephalic vein [20].

Intraoperatively, it is sometimes really hard to distinguish ectopic parathyroid tissue from usually present lymphoid and fatty tissue. Techniques such as methylene blue staining, gamma probe counter, frozen section biopsy or PTH levels monitoring can help locating the right one [17].

In vivo, parathyroid tissue is seen as yellowish-brown colored. If blood appears inside the surgical field, surrounding fatty and lymphatic tissue stains in color very similar to parathyroid tissue, which could lead to misrecognition [17, 21].

Intraoperative tissue localization using methylene blue infusion is proven helpful in approximately 80% of cases. This technique was suspected to be associated with severe adverse effects, such as neurotoxicity, especially in patients using selective serotonin reuptake inhibitors. More thorough studies, where lower doses of methylene blue solutions were used (3.5 mg/kg instead of 5–7.5 mg/kg) have proved its safety and efficiency [24]. As previously mentioned, we were not able to provide methylene blue solution, nor Geiger counter handheld probe.

Monitoring PTH levels during the surgery could confirm whether parathyroid secreting tissue has been removed (at least 50% decrease) [10]. In our patient's case, blood samples for PTH levels were collected prior to the surgery, as well as 10 minutes after removing thymus. Postoperatively, samples were taken after 12 and 24 hours. Unfortunately, these results in our case could not be obtained until the next day, so this technique did not provide us with sufficient information intraoperatively.

Practically, frozen section biopsy was the only available intraoperative monitoring. After removing the suspicious mass, which frozen section confirmed parathyroid tissue absence, we had to consider other surgical options. Knowing that the majority of mediastinal ectopic parathyroid adenomas can be found inside the thymus, our “plan B” was to perform thoracoscopic thymectomy.

There are numerous articles reporting of finding ectopic parathyroid tissue adenoma inside the thymus, as well as fewer complications in patients that were thymectomized during the initial surgery [25–28].

The final pathology report has confirmed ectopic parathyroid adenoma tissue inside the thymus, so we have avoided recurrence, consequent re-operation, and potential complications [25–28].

Postoperative revision of previously performed MRI scans was still inconclusive for precise mediastinal tumor localization.

Instead of a conclusion, we would like to underscore that if no parathyroid tissue is found during surgical exploration for parathyroid adenoma preoperatively localized in anterior mediastinum, recommendation is to think about possible intrathymic localization and consider removing the thymus. Greater sample size is necessary for higher reliability of this statement.

Conflict of interest: None declared.

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Видеоасистирана торакоскопија у случају примарног хиперпаратироидизма са аденомом локализованим унутар тимуса

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САЖЕТАК

Увод Примарни хиперпаратироидизам редак је у дечјем узрасту (2–5 : 100.000). Код преко 85% болесника присутан је аденом и његова екстирпација доводи до излечења. Код око 15–80% случајева ектопично ткиво паратироидне жлезде може се пронаћи унутар тимуса.

Приказ болесника Наш болесник био је тринаестогодишњи дечак, који је у клиничкој слици имао мултипле преломе и малаксалост. Вредности паратироидног хормона су преоперативно биле екстремно повишене (1320 pg/ml – преко 19 пута више од референтних). Вредности серумског калцијума су такође биле повишене (укупни 3,55 mmol/l; јонизовани 1,41 mmol/l). Педијатри ендокринолози су поставили дијагнозу примарног хиперпаратироидизма. После начињене преоперативне дијагностике, резултати сцинтиграфије и магнетне резонанце указивали су на постојање ектопич-

ног медијастиналног паратироидног аденома. Урађена је видеоасистирана торакоскопска тимектомија, јер после детаљне експлорације медијастинома ектопично паратироидно ткиво није пронађено. Дефинитивни патохистолошки налаз потврдио је присуство паратироидног аденома унутар тимуса.

Закључак Уколико се током експлорације медијастинома код болесника са преоперативно доказаним ектопичним паратироидним ткивом у медијастиному исти не пронађе, препорука је узети у обзир могућност његове локализације унутар тимуса, те размотрити тимектомију као начин хирушког решавања. Неопходно је истраживање на већем узорку како би се утврдила поузданост ове тврдње.

Кључне речи: примарни хиперпаратироидизам; видеоасистирана торакоскопија; тимектомија; сцинтиграфија паратироидних жлезда; деца