Health Center "Novi Sad", Novi Sad
Occupational Health Service

Case report
Prikaz slučaja
UDK 616.47-006.55-07
https://doi.org/10.2298/MPNS2404125P

THE SIGNIFICANCE OF EARLY DETECTION OF PARATHYROID ADENOMA

ZNAČAJ RANOG OTKRIVANJA ADENOMA PARATIREOIDNE ŽLEZDE

Eva STOJKOVIĆ and Tanja STEFANOVIĆ

Summary
Introduction. Parathyroid adenoma is the leading cause of primary hyperparathyroidism in 85% of cases, followed by multiglandular hyperplasia (15%) and parathyroid carcinoma (1%). Clinical complications can manifest in the bones, gastrointestinal tract, kidneys, heart, and can also lead to mental disorders and altered consciousness, including coma. Surgical intervention is the primary treatment for primary hyperparathyroidism. However, for patients who do not meet the criteria for surgery or choose to avoid it, medical management is provided. **Case Report.** A 52-year-old female patient presented in late 2019 with a visible, firm, irregular mass above the right clavicle. Initial bone marker tests raised suspicion of a parathyroid adenoma. The COVID-19 pandemic caused delays in further specialized examinations and postponed surgical treatment. The referring physician scheduled a parathyroid scintigraphy while awaiting an endocrinologist's evaluation. Surgery was eventually performed in March 2023. Despite consistently elevated parathyroid hormone and ionized calcium levels, the patient avoided potential complications due to continuous monitoring by her referring physician. **Conclusion.** Early diagnosis of parathyroid adenoma reduces the risk of complications and improves the quality of life for patients.
Key words: Parathyroid Neoplasms; Adenoma; Early Diagnosis; Hyperparathyroidism; Calcinosis

ORCID NUMBER
Eva Stojković 0000-0002-0737-3163

Sažetak
Uvod. Adenom paratireoidne žlezde je najčešći uzrok primarnog hiperparatireoidizma u 85% slučajeva, zatim multiglandularna hiperplazija (15%) i karcinom paratireoidne žlezde (1%). Kliničke komplikacije mogu nastati na kostima, gastrointestinalnom traktu, bubrezima, srcu, kao i psihički poremećaji i poremećaji svesti do kome. Lečenje primarnog hiperparatireodizma je operativno, a kod bolesnika koji ne ispunjavaju kriterijume za operativno lečenje, ili ga bolesnik ne želi, sprovodi se medikamentno lečenje. **Prikaz slučaja.** Pacijentkinja, starosti 52 godine javlja se krajem 2019. godine zbog vidljive, tvrde, nepravilne promene iznad desne ključne kosti. Urađeni su prvo koštani markeri i postavljena sumnja na adenom paratireoidne žlezde. Zbog pandemije COVID-19 u jeku, otežani su dalji specijalistički pregledi i odloženo operativno lečenje. Izabrani lekar sam zakazuje scintigrafiju paratireoidnih žlezda, čekajući mišljenje endokrinologa. Operacija je urađena u martu 2023. godine, a dotle je stanje pacijentkinje pratio izabrani lekar i uprkos konstantno povišenim vrednostima parathormona i jonizovanog kalcijuma, prevenirane su moguće brojne komplikacije adenoma. **Zaključak.** Rano postavljena dijagnoza adenoma paratireoidne žlezde omogućava smanjene nastanka komplikacija, a tako i poboljšava kvalitet života pacijenata obolelih od adenoma paratireoidnih žlezda.
Ključne reči: paratireoidne neoplazme; adenomi; rana dijagnoza; hiperparatireoidizam; kalcifikacija

Tanja Stefanović 0009-0001-3464-2779

Introduction

Primary hyperparathyroidism (HPT) is an endocrinological disorder characterized by increased secretion of parathyroid hormone (PTH) from one or more of the parathyroid glands, which are typically four in number [1]. This condition is more prevalent in women and is most commonly caused by adenomas (80-85%), with hyperplasia accounting for 10-15%, and carcinoma being a rare cause (<1%) [2]. PTH plays a crucial role in regulating calcium metabolism, which is essential for blood clotting, bone mineralization, nerve function, muscle contractions, and various enzymatic reactions.

Parathyroid adenomas are usually localized in the neck, but in up to 5% of cases, they can be ectopic. Ectopic adeno-mas may be found in the mediastinum, thymus, retropharyngeal space, submaxillary region, thyroid gland, and carotid sheath [3]. Over 90% of adenomas occur sporadically, with rare occurrences in familial hyperparathyroidism (hyperparathyroid jaw tumor syndrome) or as part of multiple endocrine neoplasia types I and II [4].

Common complications of adenomas include osteoporosis, nephrolithiasis, gastrointestinal ulcers, pancreatitis, cholelithiasis, hypertension, and heart diseases. Early diagnosis is crucial for effective management.

Case Report

A 52-year-old perimenopausal female patient, newly diagnosed with well-controlled hypertension, presented to her primary care physician in Novem-

Corresponding author: Tanja Stefanović, Dom zdravlja Novi Sad, Služba zdravstvene zaštite radnika, 21000 Novi Sad, Bulevar cara Lazara 75, E-mail: tanjastefanovic.ns@gmail.com

Abbreviations

HPT – hyperparathyroidism
PTH – parathyroid hormone
ALP – alkaline phosphatase
fT4 – free thyroxine
TSH – thyroid-stimulating hormone
25(OH)D – 25-hydroxy vitamin D
CT – computed tomography
PET/CT – positron emission tomography/computed tomography

ber 2019. She expressed concern about a palpable change above her right clavicle and reported feeling fatigued but denied other symptoms. She had a 20-year history of smoking 10 cigarettes per day, did not consume alcohol, and had no known medications or food allergies. Her mother had hypothyroidism.

On physical examination, a firm, painless mass with unclear borders and irregular shape measuring up to 1.5 cm was noted above the right clavicle, closer to the midline. Calcification was suspected and the thyroid gland was not palpable.

Initial differential diagnosis included requesting bone metabolism markers and a chest X-ray. Laboratory results were as follows: N-TACT PTH – 203.0 pg/ml (14.5-87.1 pg/ml); 25-hydroxy vitamin D (25(OH) D) – 27 nmol/l (35-120 nmol/l); crossLaps - 1,217 g/L (556-1008 g/l); total procollagen type 1 fragments – 86 ng/ml (16.3-73.9 ng/ml); alkaline phosphatase (ALP) – 93 IU/L (35-105 IU/L); ionized calcium – 2.89 mmol/L (1.00-1.35 mmol/L); inorganic phosphorus – 0.8 mmol/L (2.5-4.5 mmol/L). Both free thyroxine (fT4) and thyroid-stimulating hormone (TSH) were within reference ranges. The right clavicle X-ray showed no abnormalities. An ultrasound of the neck and upper abdomen, including the kidneys, was planned to evaluate the parathyroid adenoma, but it was delayed due to scheduling constraints.

The patient subsequently examined by an endocrinologist, who included an adenoma of the lower right parathyroid gland in the differential diagnosis. A parathyroid gland scintigraphy was requested, which the primary care physician independently arranged due to the COVID-19 pandemic and limited availability of specialist consultations.

Scintigraphy performed in February 2020 revealed a focal change in the neck and mediastinal region, suggesting an adenoma or hyperplasia of the lower right parathyroid gland. Ultrasonography indicated a separate focal change with hypo/anechoic echotexture measuring 0.8 x 1 x 1.2 cm in the lower pole and posterior right lobe of the thyroid gland, consistent with the scintigraphically isolated change. X-rays of the long bones, heart, and lungs, as well as abdominal and kidney ultrasounds, were normal. No subsequent damage was observed.

Six months post-diagnosis, follow-up laboratory tests showed: fT4 – 10.4 nmol/L (9.0-19.0 nmol/L); TSH – 0.83 mU/L (0.35-4.94 mU/L);); carcinoembryonic antigen – 0.4 ng/L (< 5 ng/ml); N-TACT-PTH – 176.0 pg/mL (14.5-87.1 pg/l); 25(OH)D total – 54 nmol/L (35-120 nmol/L); ionized calcium – 1.66 mmol/L (1.00-1.35 mmol/L); ALP – 105 IU/L (35-105 IU/L).

One year after the adenoma's discovery, the patient contracted a mild COVID-19 infection with respiratory symptoms and fever.

The patient continued to be monitored by her primary care physician, with periodic laboratory tests showing consistently elevated ionized calcium levels and PTH levels. She was prescribed oral vitamin D drops (2,500 IU/day) due to deficiency (25(OH)D total) and atorvastatin tablets (20 mg) for high cholesterol (high-density lipoprotein – 1.77 mmol/L (>1.5 mmol/L), low-density lipoprotein – 4.6 mmol/L (<3.5 mmol/L)) and an atherosclerosis index of 2.4 (<3.0).

Despite the ongoing COVID-19 pandemic, the patient waited over three years for surgical treatment. In March 2023, she underwent surgery at the University Clinical Center of Vojvodina, Clinic of Abdominal and Endocrine Surgery, where the right lower parathyroid gland was removed without complications. Histopathological examination confirmed a parathyroid adenoma measuring 0.8 x 1 cm. Postoperatively, PTH and ionized calcium levels normalized.

An osteodensitometry indicated preserved bone mineral density, with a follow-up scheduled for two years later. Chewable tablets containing calcium (500 mg) and cholecalciferol (400 IU) replaced the oral vitamin D drops. The change above the right clavicle was smaller upon inspection and palpation, and follow-up abdominal and kidney ultrasounds were normal. The patient remains in good overall condition and will continue to be monitored by her primary care physician.

Discussion

Visualizing parathyroid glands can be achieved through ultrasonography, scintigraphy, and computed tomography (CT). Scintigraphy and CT are particularly useful for diagnosing patients with ectopic parathyroid adenomas or suspected metastatic disease [5]. If ultrasonography or scintigraphy results are inconclusive, additional imaging modalities such as single-photon emission computed tomography, positron emission tomography/computed tomography (PET/CT), or Magnetic Resonance Imaging of the neck may be necessary. One potential cause of HPT is multiple endocrine neoplasia, which must be ruled out. [18F] F-choline PET)/CT is highly sensitive for detecting small parathyroid adenomas and accurately determining their location [6]. Although adenomas are most commonly localized in the neck, ectopic locations can present a significant diagnostic challenge [7].

As described, the coexistence of thyroid and parathyroid adenomas during the surgical treatment of nodular goiter underscores the importance of visualizing the parathyroid glands in preoperative preparation for successful management [8]. In this case study, a 52-year-old woman presented with generalized fatigue and a visible, palpable mass on the right side of the neck. Surgical exploration revealed a 7.7 g parathyroid adenoma, whereas adenomas typically weigh around 1 g. The uniqueness of this case lies in the fact that the adenoma was palpable as a neck mass, while the initial ultrasound suggested a thyroid nodule [9]. A review of

the literature identified 57 cases (44 in women) of spontaneous hemorrhage from parathyroid adenomas. In such cases, clinical assessment is crucial for detecting urgent conditions that may require intubation, tracheostomy, or neck exploration [10].

Detailed genomic analysis has revealed various signaling pathways, including numerous genes and proteins implicated in adenoma development. Further studies are needed to enhance our understanding of the pathogenesis of parathyroid adenomas and identify new histological biomarkers that can predict recurrence in other parathyroid glands [11].

Delayed diagnosis and treatment of parathyroid adenoma, indicated by consistently elevated serum calcium levels, significantly increases the risk of osteoporosis and secondary fractures [12].

The goal of treating asymptomatic adenoma is to prevent lesions in target organs, whereas symptomatic adenomas require timely treatment to reverse the resulting lesions.

Conclusion

The approach to managing a patient with suspected parathyroid adenoma must be comprehensive and individualized. Due to the detailed examination, the unusual localization of the observed calcification, and the immediate suspicion of a parathyroid adenoma, which was subsequently confirmed, further complications were prevented. The patient is currently in good overall condition, without nephrolithiasis, significant atherosclerotic changes, or other complications commonly associated with hyperparathyroidism, thanks to preventive measures and early detection and management.

Despite the challenges posed by the COVID-19 pandemic and the delayed surgical treatment, early diagnosis remains crucial, particularly in primary healthcare settings.

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Rad je primljen 14. VI 2024.
Recenziran 9. VII 2024.
Prihvaćen za štampu 9. VII 2024.
BIBLID.0025-8105:(2024):LXXVII:3-4:125-127.