Case Report

Coexistence of Hyperparathyroidism and Multinodular Goiter with Hashimotos Thyroiditis and Hyperthyroidism – A Rare Case Report

E.A. Ashok Kumar[1*], Bachireddy Parimala[2], Chokkavarapu Renuka Charan[2]

[1]Professor, [2]Internee
Department of General Medicine, Maheshwara Medical College and Hospital, Telangana, India
[*]Corresponding author email: **ashokedla@gmail.com**

International Archives of Integrated Medicine, Vol. 10, Issue 2, February, 2023.
Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 01-02-2023 **Accepted on:** 08-2-2023
Source of support: Nil **Conflict of interest:** None declared.

How to cite this article: E.A. Ashok Kumar, Bachireddy Parimala, Chokkavarapu Renuka Charan. Coexistence of Hyperparathyroidism and Multinodular Goiter with Hashimotos Thyroiditis and Hyperthyroidism – A Rare Case Report. IAIM, 2023; 10(2): 42-52.

Abstract

Thyroid disease and hyperparathyroidism (HPT) are among the most common endocrine disorders. Thyroid hormones play an important role in bone and calcium metabolism. The rate of HPT is greater in patients with thyroid disease than in the general medical population. Simultaneous occurrence of hyperthyroidism and hyperparathyroidism in the same patient is a rare combination. The clinical manifestations of hyperthyroidism may overshadow the more subtle and varied symptoms and signs of primary hyperparathyroidism. It poses difficult diagnostic and therapeutic problems. Both diseases, however, may have a profound influence on calcium metabolism. The resulting disturbances in thyrotoxicosis may simulate hyperparathyroidism. Contrariwise, the diagnosis of an associated parathyroid adenoma may be missed, or unnecessarily delayed because hypercalcemia is known to occur in hyperthyroidism. The coexistence of thyroiditis and thyroid nodules with parathyroid disorders is also known. Graves' disease (GD) and primary hyperparathyroidism (PHPT) are two common endocrine disorders. However the co- occurrence of hyperthyroidism and primary hyperparathyroidism (PHPT) is rare. However, the link between the two disorders remains unclarified. Hypercalcemia in Graves' hyperthyroidism should warrant a thorough investigation for concomitant primary hyperparathyroidism. Concomitant thyroid nodular disease and hyperparathyroidism (PHPT) disease has been also documented. PHPT is also reported in patients

with thyroid malignancy. We hereby report a rare case of a patient who presented with coexistence of Hyperparathyroidism and Multinodular Goiter with Hashimotos Thyroiditis and Hyperthyroidism.

Key words

Hyperparathyroidism, Multinodular goiter, Hashimotos Thyroiditis, Hyperthyroidism.

Introduction

Thyroid disease and hyperparathyroidism (HPT) are among the most common endocrine disorders [1]. The rate of HPT is greater in patients with thyroid disease than in the general medical population, and the association between these 2 pathologies has been described in several series [2-12].

1. **Hypercalcemia and Hyperthyroidism**
   Thyroid hormones play an important role in bone and calcium metabolism [13]. Coexistent thyroid pathology discovered during neck exploration in patients with PHPT has been well described [7]. In different studies, the rate of benign thyroid diseases concomitant with PHPT ranges from 17% to 84% [9, 14]. Hyperthyroidism is known to be associated with hypercalcemia.

2. **Hyperparathyroidism and Hyperthyroidism**
   Simultaneous occurrence of hyperthyroidism and hyperparathyroidism in the same patient is a rare combination which poses difficult diagnostic and therapeutic problems. The exact frequency of the association of the two diseases is unknown, but only 13 histologically proved cases have been reported [16 - 24]. The clinical manifestations of hyperthyroidism may overshadow the more subtle and varied symptoms and signs of primary hyperparathyroidism. Both diseases, however, may have a profound influence on calcium metabolism, and occasionally the resulting disturbances in thyrotoxicosis may simulate hyperparathyroidism [18]. Contrariwise, the diagnosis of an associated parathyroid adenoma may be missed, or unnecessarily delayed because hypercalcemia is known to occur in hyperthyroidism. Since hypercalcemia remains the sine qua non for the diagnosis of hyperparathyroidism, its occurrence with thyrotoxicosis demands study with regard to the known characteristics of calcium metabolism in the two diseases.

3. **Hyperparathyroidism and Hyperthyroidism with Hashimotos thyroiditis**
   It was previously reported the coexistence of thyroiditis and thyroid nodules with parathyroid disorders [25, 26].

4. **Hyperparathyroidism and Graves disease**
   Graves' disease (GD) and primary hyperparathyroidism (PHPT) are two common endocrine disorders. Thyroid hormones have effects on the regulation of bone metabolism. Mild to moderate hypercalcemia due to hyperthyroidism has been reported in approximately one in five patients [15]. However the co-occurrence of hyperthyroidism and primary hyperparathyroidism (PHPT) is rare. Noble, et al. reported a case of a 30-year-old man who had Graves' disease (GD) and PHPT. Since the 1st case of concomitant hyperthyroidism and hyperparathyroidism was reported in 1936 [27], the coexistence of GD and PHPT has been increasingly recognized by clinicians [28, 29, 30]. The development of examination methods has made the diagnosis of concurrent GD

and PHPT much easier; however, the link between the two disorders remains unclarified.

Hypercalcemia in Graves' hyperthyroidism should warrant a thorough investigation for concomitant primary hyperparathyroidism. Hypercalcemia in a patients with Graves disease can occur in up to 22% of cases [15]. The mechanism is thought to be increased bone resorption unrelated to parathyroid hormone (PTH) levels [31]. The PTH levels in hypercalcemia of thyrotoxicosis are usually suppressed or low normal. There are more rare causes of hypercalcemia in these patients with hyperthyroidism, such as hyperparathyroidism, which occurs in less than 1% of patients [32].

The presence of thyroid disease can complicate the evaluation and surgical management of patients with primary hyperparathyroidism (PHPT). Retrospective analysis has shown that approximately 20–50% of patients with PHPT also have thyroid disease [7, 34, 35].

Management of patients with PHPT and concurrent thyroid disease is an evolving field. Cases of synchronous thyroid pathology have been observed in patients presenting with primary hyperparathyroidism (PHPT), suggesting the importance of preoperative evaluation of thyroid gland [14, 36] and the development of PHPT after radioactive iodine-131 (RAI) treatment for Graves' hyperthyroidism [29, 37]. This can create a challenge in the clinical decision making and management of these patients. It is optimal to deal with both problems in one operative procedure if surgery is required [36]. However, there are fewer case reports or studies emphasizing the importance of searching for PHPT in Graves' disease patients with concomitant hypercalcemia. Here we report a unique case of hypercalcemia caused by hyperthyroidism and PHPT.

5. **Hyperparathyroidism and Hyperthyroidism with multinodular goitre and Hashimotos thyroiditis**
   Concomitant thyroid and parathyroid disease has been documented in several studies with the first report by Hellstrom in 1954. Of 50 patients evaluated for PHPT, 19 patients had thyroid nodular disease [7, 36].

6. **Hyperparathyroidism and thyroid malignancy**

The reported incidence of thyroid malignancy in patients with PHPT is approximately 3–4% [30, 32]. The association between PHPT and thyroid disease, either benign or malignant, has been documented in the literature. Indeed, up to 65% of patients with PHPT have associated thyroid abnormality [40]. Although it is rare, concomitant hyperthyroidism and PHPT in a patient should be considered, as should whether these conditions might be the result of MEN. It is well known that both MEN type 1 (MEN1) and MEN type 2A (MEN2A) may consist of neoplasia, hyperplasia, or hyper-function of the thyroid and parathyroid [41].

Case report

A 28 year old female, resident of Shivampet, Medak, Tailor by occupation came to the hospital with complaints of swelling in the anterior region of the neck, weight loss, difficulty in swallowing of 3 months duration, increased sweating of 2 months duration and cough associated with sputum of one month duration.

History of present illness

Patient was apparently asymptomatic 3months ago then she noticed of swelling in the anterior region of the neck (thyroid swelling), associated

with difficulty swallowing which was insidious in onset and gradually progressive. Patient has h/o weight loss of 3 months duration, increased sweating of 2 months duration, fatigue of 2months duration. History of breathlessness on exertion of 2 months duration. Complaints of cough associated with sputum, small in quantity, white in colour of one month duration, no history of fever, hemoptysis, loss of appetite, palpitations, chest pain or giddiness. No contact history for TB.

Past history

Not a known case of hypertension, Diabetes Mellitus, Epilepsy, Asthma, CAD, CVA. No previous surgeries.

Personal history

Appetite Normal, Mixed Diet, Digestion Normal, Bowel and Bladder Movements Regular, Sleep Adequate, No Addictions, No Allergies.

Menstrual history

Regular 3/30 days, decreased flow (1 pad/day), No clots, No dysmenorrhea.

Family history

No significant family history.

General Examination

Patient was conscious, coherent, cooperative, answering to questions well. Patient was thin built. Pallor present, No icterus, No cyanosis, No clubbing, No lymphadenopathy, No pedal edema.

Vital data

Temp - 98.60 F, Pulse -106/ min, regular, normal volume, No radio radial delay, no radio femoral delay, all peripheral pulses felt. BP- 120/60 mm Hg, Rt arm supine position. RR- 16/min.

Systemic examination

Cardiovascular system: S1 S2 Present, no murmurs heard, Respiratory system: Lungs – Clinically Clear. P/A: Soft, non tender.

Local examination

Inspection: thyroid swelling present, moving with deglutition, doesn't move with protrusion of tongue.

Palpation: Thyroid examination showed swelling in the neck - moving with deglutition, multinodular, Right lobe: 3 x 2 x 2 cm, Left lobe: 2 x 1.5 x 1 cm, small swelling over isthmus size 1x1 cm, and no bruit heard over the swelling.

Investigations

CBP-Hb-8.2 gm/dl, RBC count-4.6 millions/cumm; Total leukocyte count (TLC) was 7500/ cumm, N60, L35, M3, E3, B0, Platelet count – 2.8 lakhs/cu mm, Peripheral Smear reveals RBC – Microcytic hypochromic with few normocytic hypochromic, WBC - Relative eosinophilia, Platelets – Adequate, ESR – 50 mm/hr, Complete urine examination: colour: pale yellow, appearance: clear, pH 5.0, specific gravity: 1.030, protein : nil, glucose: nil, ketone bodies: negative, bile salts: negative, epithelial cells: 2 to 5, pus cells: 2 to 3, RBC: nil, LFT: total bilirubin: 0.4mg/dl, direct bilirubin:0.1mg/dl, indirect bilirubin: 0.3mg/dl, AST:34U/L, ALT:14U/L, ALP:103U/L, total protein:8.1g/dl, albumin: 4.1g/dl, globulin: 4.0g/dl, A/G ratio : 1, RFT: blood urea: 19mg/dl, serum creatinine: 0.6 mg/dl, Random blood sugar: 100 mg/dl, Serum Ca: 9.5, Serum phosphate: 7.9, Serum Alkaline phosphate:102 IU/L.X ray chest: lungs emphysematous, heart-normal

ECG: sinus tachycardia, Thyroid profile: Total T3 – 3.00 ng/ml (reference: 0.40 – 1.81 ng/ml), Total T4 – 20.1 ug/dl (reference: 5.5 – 11.0 ug/dl), TSH - < 0.01 u IU/ml (reference:0.4-4.2 u IU/ml), PTH – 123.6 pg/ml,(reference:15.00-68.30 pg/ml), Anti-TPO - >1000.0 (reference: <5.61 IU/ml), AntidsDNA: 11.8 (ref - 12 - 44), serum electrolytes: Na+ : 143 mmol/L, K+:3.8 mmol/L, Cl-:104 mmol/L, USG of Thyroid revealed multinodular goitre, Right lobe: 3 x 2 x 2 cm, Left lobe: 2 x 1.5 x 1 cm, small swelling over isthmus size 1x1 cm, with heterogenous echo texture and increased vascularity, enlarged bilateral inferior parathyroid glands with few cystic areas.

FNAC: impression: suggestive of nodular goiter with chronic thyroiditis, FNAC: Cytosmear studies show thyroid follicular cells arranged in sheets, few small clusters admixed with few lymphocytes against scant colloid, mixed hemorrhagic background.

Diagnosis

Hyperparathyroidism and Multinodular Goiter with Hashimotos Thyroiditis and Hyperthyroidism.

Treatment given: Patient was kept on Tab. Propythiouracil 100 mg/day.

Discussion

The coexistence of hyperthyroidism and PHPT is rare [28, 29, 42, 43, 45]. The presence of GD in patients with PHPT is now well recognized. Due to the complicated nature or non-typical clinical manifestations, the diseases are easily ignored [46]. The association of thyroid disease and PHPT is now well recognized. The occurrence of PHPT is higher in patients with thyroid disease when compared with the general population,. The incidence of synchronous thyroid abnormalities in patients with PHPT ranges from 16.6% to 84.3% [14, 36, 47]. Approximately 17–84% of patients suffering from PHPT have concomitant thyroid disease [3, 35, 48]. Wagner, et al. [3] reported a high occurrence of primary hyperparathyroidism in patients with thyroid disease (0.29%) compared with those without thyroid dysfunction (0.09%). The first report of concomitant thyroid and parathyroid disease was described by Hellstrom in 1954. Of 50 patients evaluated for PHPT, 19 patients had thyroid nodular disease [14, 39].

A recent study suggested that the coexistence rate of hyperparathyroidism and thyrotoxicosis was much higher than previously reported [32]. The association between PHPT and thyroid disease, either benign or malignant, is well documented in the literature. Up to 65% of patients with PHPT have associated thyroid abnormalities [40]. Earlier studies suggest that the risk of thyroid disease is higher in patients with PHPT. Additionally, parathyroid disease is more prevalent in patients with thyroid disease [49].

The mechanism of coexistent hyperparathyroidism and hyperthyroidism is still not clear. Some researchers believe the occurrence of this association is just a coincidence, whereas others have advocated that serum calcium level, growth factor, and genetic factors may be involved [30, 32, 49, 50, 51]. It is suggested that further studies are needed to investigate the underlying mechanism between the two disorders and their association [51]. In cases with concomitant hyperthyroidism and PHPT, the etiology for hyperthyroidism is most commonly Graves' disease [30, 47, 52, 53, 54, 55].

Whether hyperthyroidism and hyperparathyroidism occur frequently or by chance alone is still unclear. Some believed that some connections might exist between both disorders [56].

The two organs are from the same origin, i.e. branchial structures. Hence, the concomitance might occur as a part of the syndrome of multiple endocrine adenomas, resulting from the presence of the abnormal gene responsible for this syndrome [30].

Though it is rare, concomitant hyperthyroidism and PHPT in a patient should be considered, and whether these conditions might be associated with MEN. It is a well known fact that both MEN type 1 (MEN1) and MEN type 2A (MEN2A) may consist of neoplasia, hyperplasia, or hyper-function of the thyroid and parathyroid gland [41]. It is well known that Hyperthyroidism can be associated with hypercalcemia [31].

Elevated levels of interleukin (IL)-6 are seen in hyperthyroidism, and that stimulate the bone osteoclastic activity and also alter the osteoclast and osteoblast coupling [31].

Triiodothyronine is known to increase the sensitivity of bone to IL-6 [31]. Hyperparathyroidism should be considered in the differential diagnosis of a patient presenting with hypercalcemia, even in those presenting with hyperthyroidism. PTH levels are useful to differentiate these cases because in hypercalcemia solely due to hyperthyroidism, the PTH level is usually suppressed [32]. Hyperparathyroidism might be produced due to a long-standing effect of excess thyroid hormone on adrenergic receptors [56].

There is no known correlation of MEN 1 with Graves disease. Hypercalcemia may occur in hyperthyroidism and may mask concomitant PHPT. Thus, if hypercalcemia persists after treatment of hyperthyroidism with high or unsuppressed PTH levels, this should indicate PHPT. To avoid repeated surgery and complications, it is necessary to evaluate parathyroid disease in hypercalcemic patients with Graves Disease. In addition, some hormones, such as adrenaline and glucocorticoid hormones, are dysregulated under hyperthyroid conditions, thereby contributing to a hypercalcemic state [53].

Increased serum ALP level was found in approximately 50% of the patients with hyperthyroidism complicated with hypercalcemia [57, 58, 59]. The serum calcium level is usually normal in hyperthyroidism, but hypercalcemia accompanying thyrotoxicosis has been noted with increasing frequency since it was first reported in 1936 [18]. The increased resorption of bone in hyperthyroidism may lead to an excessive excretion of calcium and phosphorus in the urine and may cause osteoporosis of severe degree so as to result in spontaneous pathologic fractures [60]. With control of the thyroid hyperfunction, however, the elevated serum calcium of thyrotoxicosis has been found to return to normal [61]. In other reported cases of simultaneous hyperthyroidism and hyperparathyroidism, there was persistence of hypercalcemia after adequate treatment of the hyperthyroidism. It is a strong indication for surgical exploration of the parathyroid glands.

Persistence of hypercalcemia after the normalization of TSH, however, is suggestive of other etiologies for hypercalcemia and work-up of PHPT is warranted. The diagnosis of primary hyperparathyroidism is suggested by high calcium and non-suppressed iPTH level [62].

The prevalence of hypercalcemia with hyperthyroidism has been reported to be 17 to 50% [15, 40, 63, 64, 49, 1-3, 5]. The true prevalence may be difficult to evaluate for two reasons. First, serum calcium concentrations is not routinely measured in non acute settings of thyrotoxicosis [2]. Second, most of the cases with hypercalcemia in the setting of hyperthyroidism may also have other comorbid illnesses, like diabetes insipidus [58, 66, 67], renal insufficiency [67], or concurrent hyperparathyroidism [40], factors that could confuse the overall metabolic picture.

Patients with thyroid disease should undergo analysis of serum calcium and PTH levels to check for underlying parathyroid disease. Patients with PHPT should undergo neck ultrasound to detect thyroid nodules and subsequent FNAC if indicated to assess for malignancy. Detection of concomitant disease pre - operatively can help guide surgical planning, decrease post-operative complications of undetected disease, and minimize the need for reoperation [49].

Evaluation of goiter usually involves imaging modalities like ultrasonography, CT scans or magnetic resonance imaging [49]. The presence of thyroid disease can complicate the evaluation and surgical management of patients with primary hyperparathyroidism (PHPT) [68].

A possibility is that the mononuclear inflammatory infiltrate in the thyroid gland associated with Hashimoto’s disease irritated the neighboring parathyroid gland parenchyma and caused a transient release of PTH. Indeed, the

parathyroid gland is frequently embedded in the capsule of the thyroid gland, and hyperparathyroidism has been reported in association with thyroid disorders [10]. Thus, local irritation might be one explanation for transient hyperparathyroidism.

Subclinical hyperparathyroidism would represent the earliest manifestation of primary hyperparathyroidism, the elusive initial phase of the disease [69]. Silverberg SJ et al report a case where in it indicates, that the elevated PTH level may be transient, especially in patients with coexistent thyroid disorders, such as Hashimoto's thyroiditis. In such patients, close follow-up is recommended.

The rare presentation in our patient was of Hyperparathyroidism and Multinodular Goiter with Hashimotos Thyroiditis and Hyperthyroidism. We started antithyroid medications in our patient.

Conclusion

The coexistence of hyperthyroidism and PHPT is now well recognized. The coexistence of thyroiditis and thyroid nodules or MNG with parathyroid disorders is also described. The coexistence of GD and PHPT has also been increasingly recognized. The presence of thyroid disease can complicate the evaluation and surgical management of patients with primary hyperparathyroidism (PHPT). The thyroid malignancy in patients with PHPT is also documented. It is well known that both MEN type 1 (MEN1) and MEN type 2A (MEN2A) may consist of neoplasia, hyperplasia, or hyperfunction of the thyroid and parathyroid glands. The mechanism of coexistent hyperparathyroidism and hyperthyroidism is still not clear. Persistence of hypercalcemia after the normalization of TSH, however, is suggestive of other etiologies for hypercalcemia and work-up of PHPT is warranted. The diagnosis of primary hyperparathyroidism is suggested by high calcium and non-suppressed iPTH level. Hypercalcemia in patients with hyperthyroidism, should undergo investigation for concomitant primary hyperparathyroidism that would facilitate the treatment modality.

We herewith report a rare case of Coexistence of Hyperparathyroidism and Multinodular Goiter with Hashimotos Thyroiditis and Hyperthyroidism. This patient initially presented with hyperthyroidism and hypercalcemia. On evaluation, USG and FNAC, of thyroid revealed enlarged parathyroid glands with multinodular goiter, with Hashimatos thyroiditis and increased PTH levels.

References

1. Golden SH, Robinson KA, Saldanha I, et al. Clinical review: Prevalence and incidence of endocrine and metabolic disorders in the United States: A comprehensive review. J Clin Endocrinol Metab., 2009; 94: 1853.
2. Stoffer SS, Szpunar WE, Block M. Hyperparathyroidism and thyroid disease: A study of their association. Postgrad Med., 1982; 71: 91.
3. Wagner B, Begic-Karup S, Raber W, et al. Prevalence of primary hyperparathyroidism in 13,387 patients with thyroid diseases, newly diagnosed by screening of serum calcium. Exp Clin Endocrinol Diabetes, 1999; 107: 457.
4. Regal M, Pa´ramo C, Luna Cano R, et al. Coexistence of primary hyperparathyroidism and thyroid disease. J Endocrinol Invest., 1999; 22: 191.
5. Strichartz SD, Giuliano AE. The operative management of coexisting thyroid and parathyroid disease. Arch Surg., 1990; 125: 1327.
6. Attie JN, Vardhan R. Association of hyperparathyroidism with non-medullary thyroid carcinoma: Review of 31 cases. Head Neck, 1993; 15: 20.
7. Sidhu S., Campbell P. Thyroid pathology associated with primary hyperparathyroidism. Australian and

New Zealand Journal of Surgery, 2000; 70(4): 285-287.

8. Zheng YX, Xu SM, Wang P, et al. Preoperative localization and minimally invasive management of primary hyperparathyroidism concomitant with thyroid disease. J Zhejiang Univ Sci B, 2007; 8: 626.
9. Kösem M., Algün E., Kotan C., Harman M., Öztürk M. Coexistent thyroid pathologies and high rate of papillary cancer in patients with primary hyperparathyroidism: controversies about minimal invasive parathyroid surgery. Acta Chirurgica Belgica, 2004; 104(5): 568-571.
10. Sianesi M, Del Rio P, Arcuri MF, et al. Hyperparathyroidism associated with thyroid pathology. Am J Surg., 2003; 185: 58- 60.
11. Del Rio P, Arcuri MF, Bezer L, et al. Association between primary hyperparathyroidism and thyroid disease: Role of preoperative PTH. Ann Ital Chir., 2009; 80: 435.
12. Katz AD, Kong LB. Incidental preclinical hyperparathyroidism identified during thyroid operations. Am Surg., 1992; 58: 747.
13. Işılay Kalan Sari, Ramazan Coşar, Şenay Arikan. Hypercalcemia due to Primary Hyperparathyroidism in a patient with Graves' disease. Tıp Fak Derg., 2022; 24(1): 192-196.
14. Morita S. Y., Somervell H., Umbricht C. B., Dackiw A. P., Zeiger M. A. Evaluation for concomitant thyroid nodules and primary hyperparathyroidism in patients undergoing parathyroidectomy or thyroidectomy. Surgery, 2008; 144(6): 862-866 discussion 866-8.
15. Baxter JD, Bondy P. Hypercalcemia of thyrotoxicosis. Ann Intern Med., 1966; 65: 429–442.
16. Bortz W., E. Eisenberg, C. Bowers, M. Pont. Differentiation between Thyroid and Parathyroid Causes of Hypercalceria. Ann.Intern. Med., 1961; 54: 610.
17. Frame B., R. H. Durham. Simultaneous Hyperthyroidism and Hyperparathyroidism. Amer. J. Med., 1959; 27: 824.
18. Gadeholt H. Simultaneous Hyperparathyroidism and Graves' Disease. Acta Med. Scand., 1961; 169: 283.
19. Hubble D. Skeletal Manifestations of Gen-eral Disease. Proc. Roy. Soc. Med., 1958; 51: 475.
20. Jackson C. E., J. S. Webster, P. C. Talbert, H. D. Caylor. Concomitant Hyperpara-thyroidism as a Cause of the Hypercalcemia Associated with Hyperthyroidism. Ann. In-ter. Med., 1961; 54: 992.
21. Koenig M. P., D. A. Scholz, R. M. Salassa. Hypercalcemia in Hyperthyroidism. Minnesota Med., 1957; 40: 782.
22. Miller E. S., L. R. Evans. Simultaneous Hyperfunction of the Thyroid and Para-thyroid Glands. New Engl. J. Med., 1942; 227: 949.
23. Noble J. F., J. F. Borg. Hyperparathyroidism Complicated by Hyperthyroidism. Arch. Int. Med., 1932; 58: 846.
24. Ramsdell J. A., B. M. Black, L. B. Woolner, F. R. Keating. Tumors of the Parathyroid Glands Found Incidentally During Surgical Procedures. Surg. Gynec. & Obst., 1960; 111: 451.
25. Huang C, Wang X. Subacute thyroiditis manifesting as a thyroid mass, vocal cord paralysis, and hypercalcemia. Endocr Pract., 2012; 18(2): e17-20.
26. Farooki A, Wang X. Transient subclinical hyperparathyroidism in a patient with hashimoto's thyroiditis. Endocr Pract., 2006; 12(3): 338-340.
27. Noble JF, Borg JF. Hyperparathyroidism complicated by hyperthyroidism. Report of a case. Arch Int Med., 1936; 58: 846-59.

28. Abboud B, Sleilaty G, Mansour E, El Ghoul R, Tohme C, Noun R, Sarkis R. Prevalence and risk factors for primary hyperparathyroidism in hyperthyroid patients. Head Neck, 2006; 28: 420-6.
29. Wei S, Baloch ZW. LiVolsi VA. Parathyroid adenoma in patients with Graves' disease: a report of 21 cases. Endocr Pathol., 2015; 26: 71-4.
30. Xiao H, Yu B, Wang S, Chen G. Concomitant Graves' disease and primary hyperparathyroidism: the first case report in mainland of China and literature review. Chin Med J (Engl), 2002; 115: 939-41.
31. Akalin A, Colak O, Alatas O, Efe B. Bone remodeling markers and serum cytokines in patients with hyperthyroidism. Clin Endocrinol (Oxf), 2002; 57: 125–129.
32. McGowan DM, Vaswani A, Shperling I. Coexisting hyperparathyroidism with thyrotoxicosis. J Endocrinol Invest., 1991; 14: 305–310.
33. Kairys JC, Daskalakis C, Weigel RJ. Surgeon-performed ultrasound for preoperative localization of abnormal parathyroid glands in patients with primary hyperparathyroidism. World J Surg., 2006; 30: 1658–63.
34. Adler JT, Chen H, Schaefer S, Sippel RS. Does routine use of ultrasound result in additional thyroid procedures in patients with primary hyperparathyroidism? J Am Coll Surg., 2010; 211: 536–9.
35. Heizmann O, Viehl CT, Schmid R, et al. Impact of concomitant thyroid pathology on preoperative workup for primary hyperparathyroidism. Eur J Med Res., 2009; 14: 37–41.
36. Beus KS, Stack BC. Synchronous thyroid pathology in patients presenting with primary hyperparathyroidism. Am J Otolaryngol., 2004; 25(5): 308-312.
37. Wang X, Renedo MF. Graves' disease occurring after hyperparathyroidism and subacute thyroiditis. Endor Pract., 2004; 10(6): 509-511.
38. Koh E, Kim D, Wang X. Case series of hyperparathyroidism associated 131 RAl for Grave's disease. Endor Rev., 2011; 32: P1-P243.
39. Hellstrom J. Primary hyperparathyroidism; observations in a series of 50 cases. Acta Endocrinol (Copenh), 1954; 16: 30-58.
40. Toursarkissian B, Sloan DA, Schwartz RW. Coexisting hyperthyroidism and primary hyperparathyroidism. Surgery, 1993; 113(6): 716-718.
41. Thakker RV, Newey PJ, Walls GV, Bilezikian J, Dralle H, Ebeling PR, Melmed S, Sakurai A, Tonelli F, Brandi ML. Endocrine Society. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). J Clin Endocrinol Metab., 2012; 97: 2990-3011.
42. Arem R, Lim-Abrahan MA, Mallette LE. Concomitant Graves' disease and primary hyperparathyroidism. Influence of hyperthyroidism on serum calcium and parathyroid hormone. Am J Med., 1986; 80(4): 693-8.
43. Cai X, Yousefzadeh P, Wang X. Hypercalcemia caused by concomitant Graves disease and primary hyperparathyroidism. J Endocrinol Thyroid Res., 2018; 3(1): 555603.
44. Thalhammer M, Cuk A, Pitzl H, Palitzsch KD. Concomitant Graves' disease and primary hyperparathyroidism: clinical implications and preoperative localization of parathyroid adenoma by fine needle biopsy. CEJ Med., 2006; 1(3): 298-305.
45. Miani C, Bracale AM, Bresadola V, Motz E. Concomitant primary hyperparathyroidism, Graves' disease and vitamin D deficiency. Acta Otorhinolaryngol Ital., 2003; 23(3): 199-202.

46. Fang Zhang, Xiaohui Pan, Nanwei Tong, Qingguo Lü. Coexistence of Graves' disease and primary hyperparathyroidism: a case description. Quant Imaging Med Surg., 2022; 12(5): 3014-3019.
47. Goldfarb M, O Neal P, Shih JL, Hartzband P, Connolly J, Hasselgren PO. Synchronous parathyroid carcinoma, parathyroid adenoma, and papillary thyroid carcinoma in a patient with severe and long-standing hyperparathyroidism. Endocr Pract., 2009; 15(5): 463-8.
48. Spanheimer PM, Weigel RJ. Management of patients with primary hyperparathyroidism and concurrent thyroid disease: an evolving field. Ann Surg Oncol., 2012; 19(5): 1428–9.
49. Wright MC, Jensen K, Mohamed H, Drake C, Mohsin K, Monlezun D, Alsaleh N, Kandil E. Concomitant thyroid disease and primary hyperparathyroidism in patients undergoing parathyroidectomy or thyroidectomy. Gland Surg., 2017; 6(4): 368-374.
50. He Y, Liu S, Guo H, Shi B. Incidental finding of papillary thyroid carcinoma with BRAFV600E mutation in a patient with coexistent primary hyperparathyroidism and Graves' hyperthyroidism. BMJ Case Rep., 2014; 2014: bcr2013203436, PMID 24879726, PMCID: PMC4039927.
51. Klemm T, Lamesch P, Paschke R. Coincidence of hot thyroid nodules and primary hyperparathyroidism. Exp Clin Endocrinol Diabetes, 1999; 107: 295-8.
52. Nagaki S, Tachikawa E, Kodama H, Obara T, Osawa M, Nagata S. A case of Turner's syndrome with Graves' disease and primary hyperparathyroidism. SAGE Open Med Case Rep., 2021; 9: 2050313X211059002.
53. Yokomoto M, Minamoto M, Utsunomiya D, Umakoshi H, Fukuoka T, Kondo S. Hypercalcemic crisis due to primary hyperparathyroidism occurring concomitantly with Graves' disease. Intern Med., 2015; 54(7): 813–8.
54. He Y, Liu S, Guo H, Shi B. Incidental finding of papillary thyroid carcinoma with BRAFV600E mutation in a patient with coexistent primary hyperparathyroidism and Graves' hyperthyroidism. BMJ Case Rep., 2014: bcr2013203436.
55. Tachibana S, Sato S, Yokoi T, Nagaishi R, Akehi Y, Yanase T, et al. Severe hypocalcemia complicated by postsurgical hypoparathyroidism and hungry bone syndrome in a patient with primary hyperparathyroidism, Graves' disease, and acromegaly. Intern Med., 2012; 51(14): 1869–73.
56. Barsotti MM, Targovnik JH, Verso TA. Thyrotoxicosis, hypercalcemia, and secondary hyperparathyroidism. Arch Intern Med., 1979; 139: 661-663.
57. Iqbal AA, Burgess EH, Gallina DL, et al. Hypercalcemia in hyperthyroidism: patterns of serum calcium, parathyroid hormone, and 1,25-dihydroxyvitamin d3 levels during management of thyrotoxicosis. Endocr Pract., 2003; 9: 517–21.
58. Endo A, Shigemasa C, Kouchi T, et al. Development of hypercalcemic crisis in a Graves' hyperthyroid patient associated with central diabetes insipidus. Intern Med., 1995; 34: 924–8.
59. Parker KI, Loftley A, Charles C, et al. A case of apathetic thyroid storm with resultant hyperthyroidism-induced hypercalcemia. Am J Med Sci., 2013; 346: 338–40.
60. Dunlap, H. F. Cases Showing Osteoporosis Due to Decalcification in Exophthalmic Goiter. Proc. Mayo Clin., 1928; 3: 119.
61. Bortz W., E. Eisenberg, C. Bowers, M. Pont. Differentiation between Thyroid and Parathyroid Causes of Hypercalcemia. Ann. Intern. Med., 1961; 54: 610.

62. Xinjiang C, Pegah Y, Xiangbing W. Hypercalcemia Caused By Concomitant Graves Disease and Primary Hyperparathyroidism. J Endocrinol Thyroid Res., 2018; 3(1): 555603.
63. Gordon DL, Suvanich S, Erviti V, Schwartz MA, Martinez CJ. The serum calcium level and its significance in hyperthyroidism: a prospective study. Am J Med Sci., 1974; 268: 31-36.
64. Hayes JR, Ritchie CM. Hypercalcemia due to thyrotoxicosis. Ir J Med Sci., 1983; 152: 422-423.
65. Mosekilde L, Christensen S. Decreased parathyroid func- tion in hyperthyroidism: interrelationships between serum parathyroid hormone, calcium-phosphorus metabolism and thyroid function. Acta Endocrinol (Copenh)., 1977; 84: 566- 575.
66. Wada S, Kurihara S, Imamaki K, et al. Hypercalcemia accompanied by hypothalamic hypopituitarism, central diabetes insipidus and hyperthyroidism. Intern Med., 1999; 36: 486-490.
67. Reuler JB, Wise RW, Thorpe JB. Anemia, renal insufficiency, and hypercalcemia in a man with hyperthyroidism. South Med J., 1985; 78: 59-63, 68.
68. Philip M. Spanheimer, Ronald J. Weigel. Management of Patients with Primary Hyperparathyroidism and Concurrent Thyroid Disease: An Evolving Field. Ann Surg Oncol., 2012; 19: 1428–1429.
69. Silverberg SJ, Bilezikian JP. "Incipient" primary hyper- parathyroidism: a "forme fruste" of an old disease. J Clin Endocrinol Metab., 2003; 88: 5348-5352.