Atrial Fibrillation and Thyrotoxicosis Following Parathyroidectomy

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Hyperparathyroidism is one of the most common endocrinopathies. Surgical resection is considered to be the gold standard and carries a 95% cure rate and an extremely low complication rate [1]. Transient hyperthyroidism is noted in up to 30% of parathyroidectomy surgeries; however, thyrotoxicosis is a rare phenomenon. Most reported cases are mild and self-limited [2]. Atrial fibrillation (AF) as part of thyrotoxicosis following parathyroidectomy is even rarer [3,4]. We describe two cases of thyrotoxicosis with new onset AF following parathyroidectomy and present a review of the existing literature. Surgeons and endocrinologists should be aware of this possible and rare complication following parathyroidectomy.

PATIENT DESCRIPTION

PATIENT 1

A 38-year-old male with nephrolithiasis was diagnosed with primary hyperparathyroidism. Past medical history was positive for a history of gout treated by colchicine. Indications for surgery were young age and nephrolithiasis. The patient underwent minimally invasive parathyroidectomy, and the right upper parathyroid gland was resected. Intraoperative parathyroid hormone (PTH) levels dropped from 14 to 3.6 pmol/L (normal range 1.26–6.84 pmol/L) and the patient was discharged home on postoperative day one with a calcium level of 2.27 mmol/L (normal range 2.15–2.55). Pathology was compatible with a parathyroid adenoma measuring 3.7 × 1.5 × 0.8 cm and weighing 2.6 grams.

Two days after surgery the patient returned to our department complaining of paresthesia in both hands and feet. His PTH level was 0.7 pmol/L (low) and calcium was 2.2 mmol/L (normal). The patient was treated with oral calcium and was referred to the outpatient clinic for follow-up. In the evening of the same day, he returned complaining of palpitations and dyspnea without chest pain. On further questioning and physical examination, there were no other symptoms or signs of hyperthyroidism. His pulse was 118/minute, irregularly irregular, and blood pressure 131/83 mmHg. An electrocardiogram showed AF. Laboratory results were significant for a decreased thyroid stimulating hormone (TSH) 0.27 MU/L (normal 0.5–4.5) and an elevated free T4 (FT4) 31.67 pmol/L (normal range 10.2–19.7), compatible with thyrotoxicosis. Anticoagulation with subcutaneous low-molecular weight fractioned heparin (LMW-FH) (enoxaparin) was started. He was successfully treated with a loading protocol of amiodarone and returned to sinus rhythm within 12 hours. He felt resolution of symptoms and was discharged later that day, with a prescription of beta-blocker. Given a low $CHA_2DS\text{-}VAS_2C$ score of 0, a reversible trigger and a single AF episode, anticoagulation was stopped. Thyroid function tests normalized within a few weeks [Figure 1A].

Two years after the operation the patient had not had recurrent arrhythmia or symptoms of hyperthyroidism. His calcium and PTH, TSH, and FT4 levels remained within normal limits.

PATIENT 2

A 66-year-old woman who had primary hyperparathyroidism for 6 years was referred for parathyroidectomy. Indication for surgery was based on presence of symptomatic hypercalcemia (weakness and muscle ache) and osteoporosis.

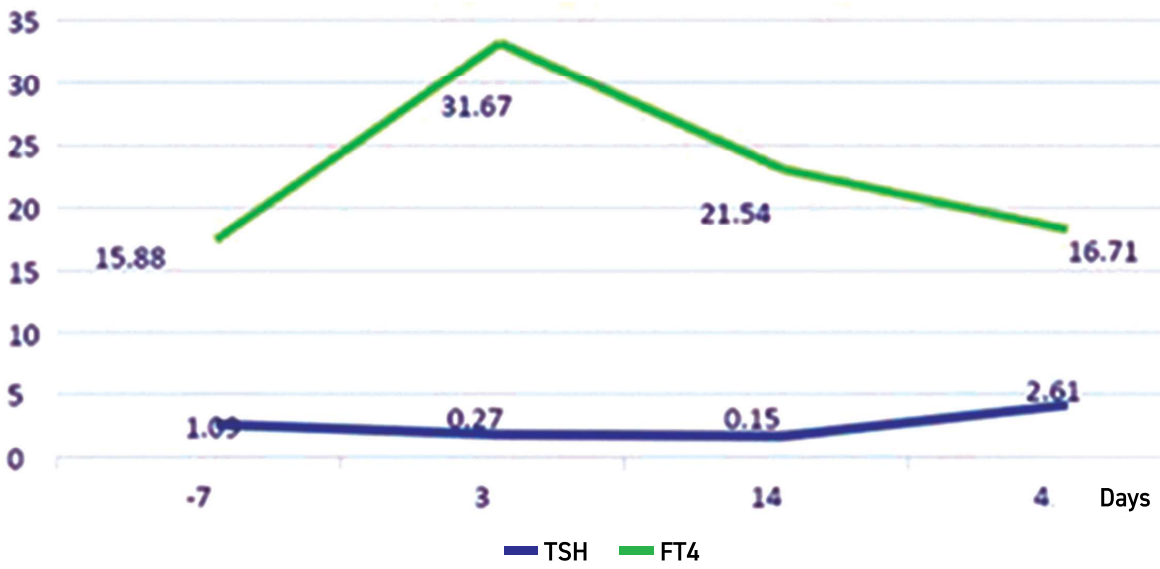
Due to a suspicion of bilateral parathyroid findings on preoperative imaging, bilateral exploration was performed. An enlarged right upper parathyroid gland was identified and resected, and intraoperative PTH levels dropped from 17.2 to 4 pmol/L (1.26–6.84). The patient was discharged home on postoperative day one with a calcium level of 2.23 mmol/L (normal range 2.15–2.55). Pathology was compatible with a parathyroid adenoma measuring 2.1 × 1.6 × 1.4 cm and weighing 2.4 grams.

On postoperative day 3, the patient arrived at the emergency department, complaining of palpitations, which had started 6 hours prior to admission, dizziness, and headache. She denied chest pain or dyspnea. Vital signs revealed an irregular tachycardia with a pulse of 96/minute and blood pressure 143/84 mmHg. An electrocardiogram showed AF. Basic laboratory results were normal with the exclusion of C-reactive protein of 1.8 (normal > 0.5). Anticoagulation was

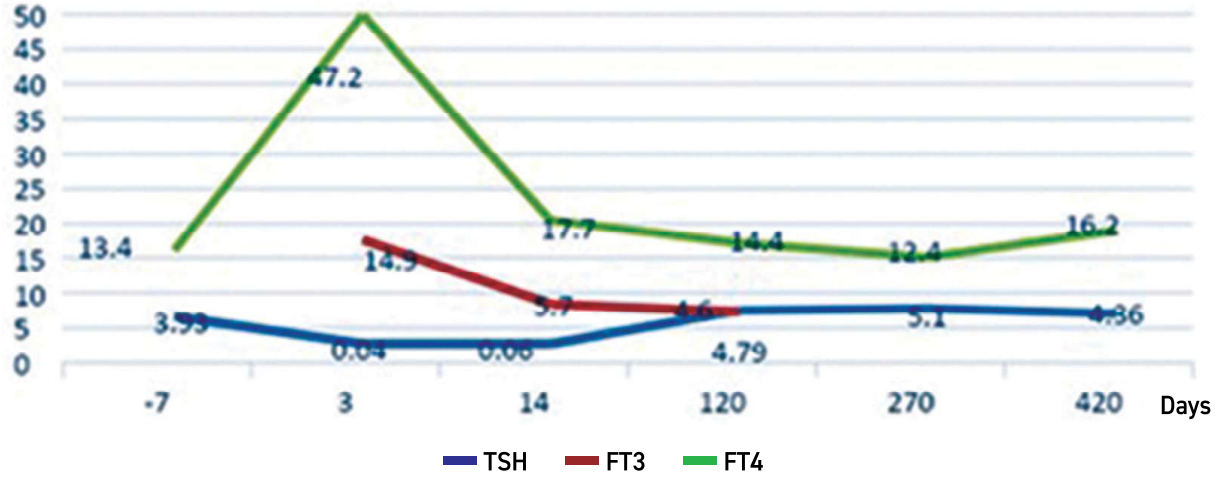
Figure 1. Dynamic follow-up of the laboratory thyroid function test with thyrotoxicosis following parathyroidectomy. FT4 normal range 10–20 pmol/L; FT3 normal range 3.5–6.5 pmol/L; TSH normal range 0.55–4.78 Mu/L

FT4 = free T4, TSH = thyrotropin

[A] Patient 1



[B] Patient 2



initiated and propafenone administered, successfully converting the patient to sinus rhythm. Once her cardiac rhythm normalized, her clinical condition improved. For similar reasons as in the previous case, anticoagulation was stopped.

As a standard workup evaluation of new onset of AF, a thyroid function test was performed and revealed thyrotoxicosis with decreased TSH 0.04 MU/L (normal 0.5–4.5) and an elevated FT4 47.2 pmol/L (normal range 10.2–19.7) as well as FT3 14.9 (normal 3.5–6.5). During follow-up [Figure 1B] her thyroid function rapidly improved but she also developed a subclinical hypothyroidism up to 9 months after the thyrotoxicosis event and finally turned to be clinically and laboratory euthyroid.

COMMENT

We describe two cases of AF in context of thyrotoxicosis following very recent

parathyroidectomy. In both patients there were no risk factors predisposing to AF except thyrotoxicosis. Both surgeries were performed without complications. Only one parathyroid gland was resected in both patients. Patient 2 had bilateral neck exploration. The treatment of AF was different in the two patients, loading protocol of amiodarone vs. propafenone; nevertheless, both treatments achieved resolution of AF. In both patients, thyrotoxicosis spontaneously resolved, but in patient 2 a prolonged period of subclinical hypothyroidism was observed.

Transient thyrotoxicosis after parathyroidectomy is an uncommon complication. It was first described in a case series in 1992 [2]. Thyrotoxicosis appeared within 2 weeks of surgery, characterized by minor symptoms, which self-resolved within 4–6 weeks. It was assumed to be related to thyroid gland manipulation (and subsequent release of thyroid hormone into the blood stream). It was advised to minimize exploration during parathyroid surgery.

A limited number of case reports have appeared in the literature [2]. The clinical manifestation includes sweating, heat intolerance, palpitation, tachycardia, and other hyperthyroidism symptoms. Only two significant cardiac complications of thyrotoxicosis were described: one of myocardial infarction [3] and one of AF [4]. Both events happened to patients who underwent parathyroidectomy for secondary hyperparathyroidism (sHPT) due to chronic renal failure.

AF is a common cardiac manifestation of thyrotoxicosis. It happens in 10–15% of hyperthyroid patients depending on the underlying cause. In a population-based study of 40,628 patients with clinical hyperthyroidism, 8.3% had AF or flutter [5]. Hyperthyroidism is known to cause atrial premature beats, non-sustained supraventricular tachycardia, and increased heart rate. Correlation has been shown between the presence of AF and the duration and biochemical severity of hyperthyroidism [5]. Parathyroidectomy-related thyrotoxicosis is a subgroup of thyrotoxicosis characterized by transient and mild hyperthyroidism, which can explain it is rarely diagnosed and described.

From a clinical point of view, parathyroidectomy-related thyrotoxicosis is a challenging syndrome. It should be highly suspected in patients within 2 weeks post-parathyroidectomy to avoid unnecessary investigation and to address and relieve symptoms. In our opinion, there is no need for routine TSH level monitoring if a patient is asymptomatic.

CONCLUSIONS

Post-parathyroidectomy thyrotoxicosis was thought to be an uncommon syndrome with no significant clinical consequences. Clinicians must be aware of the phenomenon and educate their patients to seek medical attention with any signs of angina, dyspnea, palpitations, or other typical signs of thyrotoxicosis.

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Capsule

An immunodominant $NP_{105-113}$-B*07:02 cytotoxic T cell response controls viral replication and is associated with less severe COVID-19 disease

$NP_{105–113}$-B*07:02-specific CD8+ T cell responses are considered among the most dominant in SARS-CoV-2-infected individuals. **Peng** et al. found strong association of this response with mild disease. Analysis of $NP_{105–113}$-B*07:02-specific T cell clones and single-cell sequencing were performed concurrently, with functional avidity and antiviral efficacy assessed using an in vitro SARS-CoV-2 infection system, and were correlated with T cell receptor usage, transcriptome signature and disease severity (acute n=77, convalescent n=52). The authors demonstrated a beneficial association of $NP_{105–113}$-B*07:02-specific T cells in COVID-19 disease progression, linked with expansion of T cell precursors, high functional avidity and antiviral effector function. Broad immune memory pools were narrowed post-infection but $NP_{105–113}$-B*07:02-specific T cells were maintained 6 months after infection with preserved antiviral efficacy to the SARS-CoV-2 Victoria strain, as well as Alpha, Beta, Gamma, and Delta variants. The data show that $NP_{105–113}$-B*07:02-specific T cell responses associate with mild disease and high antiviral efficacy, pointing to inclusion for future vaccine design.

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