

Case Series

A case series on the determination of pre-operative risk factors for anticipation of post operative hypocalcaemia in thyroidectomy

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ABSTRACT

During thyroidectomy, careful dissection of the parathyroid and tracing of their blood supply is the dictum. But it may not always be possible. We aim to highlight some of the common situations faced by ENT surgeons during thyroidectomy, where intraoperative identification and preservation of either the parathyroid glands or their blood supply may be difficult or the glands may have to be sacrificed. We wish to highlight 5 cases where hypocalcemic tetany occurred after total thyroidectomy and pre operative anticipation of their risk factors and the reasoning for the same. Extra precaution should be taken to try and identify and preserve at least one parathyroid gland to prevent lifelong morbidity due to hypocalcemia. Additionally, one must be on the lookout for such challenging cases preoperatively and appropriate consent should be taken from the patient.

Keywords: Thyroidectomy, Parathyroid, Hypocalcemia, Hypoparathyroidism, Calcium

INTRODUCTION

Thyroidectomy is one of the commonest surgeries performed worldwide. Surgery is done for suspicious and malignant nodules or may be considered for growing nodules that are benign after repeat fine needle aspiration (FNA) if they are large (>4 cm), causing compressive or structural symptoms, or based upon clinical concern.¹

Although generally considered safe, the two most common complications include recurrent laryngeal nerve injury and hypoparathyroidism. Other documented complications include post operative haemorrhage, minor dysphagia, thoracic duct injury, tracheal or oesophageal wounds, Horner's syndrome and hypertrophic scars. Temporary dysphonia due to nerve injury occurs in 5-11% of cases and may be permanent in 1 to 3.5% of cases, and temporary hypoparathyroidism due to

parathyroid injury occurs in 20 to 30% of cases and may be permanent in 1 to 4% of cases.²

Hypocalcemia is a medical condition characterized by low calcium levels in the blood serum. The normal range of blood calcium is typically between 2.1-2.6 mmol/l (8.8-10.7 mg/dl, 4.3-5.2 mEq/l) while levels less than 2.12 mmol/l are defined as hypocalcemia.³ Hypocalcemia becomes clinically apparent with tetany at serum concentration 35% below normal includes muscular spasms (tetany) and perioral tingling, Chvostek's sign and Trousseau's sign.⁴

Hypoparathyroidism (and hence hypocalcemia) is mostly seen following inadvertent excision of or damage to the parathyroid glands or their vascular supply during a total thyroidectomy. While most cases are transient, permanent/persistent hypocalcemia is defined if symptoms persist for more than 6 months after surgery.³

The aim of this case series is to enlighten clinicians of 5 cases where hypocalcemic tetany occurred after total thyroidectomy and the risk factors and how to prevent the same.

CASE SERIES

Case 1

A 43-year-old female presented to ENT department with diffuse neck swelling, palpitations and tremors (Figure 1). She was on carbimazole and propranolol for previously diagnosed hyperthyroidism. Examination showed a diffuse thyroid swelling moving with deglutition. No lymphadenopathy was noted. A thyroid profile was done which showed TSH levels of 0.02 mIU/l. The dose of carbimazole was increased from 10mg 12 hourly to 20 mg 12 hourly and the patient was reevaluated at the end of 6 weeks, once the clinical signs of thyrotoxicosis had subsided. A repeat thyroid profile showed normal TSH levels. The ultrasonography (USG) and FNA findings were both consistent with a TIRADS 2, BETHESDA II multinodular goitre, the largest being 3×4 cm. Anti thyroid antibodies were negative, and a decision was taken to undertake total thyroidectomy to relieve the compressive symptoms of the patient as well as, as per the patients request, improve her aesthetic appearance.

Since the parathyroid glands could not be properly identified during the surgery, the patient was initially started on empirical oral calcium (500 mg TID), and was later shifted over to intravenous calcium gluconate (2 gm per day) when symptoms of hypocalcemia set in. After 4 days of IV calcium gluconate, one the symptoms of hypocalcemia subsided, she was switched back to oral calcium and was discharged with the same. Oral calcium was continued for 3 weeks post operatively after which she was gradually tapered off.



Figure 1: Patient with multinodular goitre, and exophthalmos.

Case 2

A 42-year-old woman presented with a thyroid swelling in front of her neck since 1 year. It was insidious in onset and gradually progressive. She was euthyroid and no respiratory distress at the time of presentation. There was no history of palpitation or tremors. USG showed a 19x75mm TIRADS 4 spongiform nodule in the right lobe of thyroid, with another suspicious sub centimetric nodule in the contralateral lobe. FNA from the right lobe was consistent with BETHESDA VI papillary carcinoma. She underwent total thyroidectomy. On the third post operative day, she started showing features of hypoparathyroidism and was started on oral calcium (500 mg TID). Once the features subsided, the patient was discharged on a maintenance dose of 500 mg OD calcium for 2 weeks.

Case 3

A 47-year-old female presented to ENT OPD with 5-year long history of a neck swelling (Figure 2). She was also complaining of difficulty in breathing. She was on treatment for hyperthyroidism for the past 10 years. She had type II diabetes mellitus and hypertension for 5 years, which were under good control with medications. The size of the neck swelling was increasing gradually but the patient complained about the rapid increase in size for the past 2 years. The USG was showed a hyperechoic heterogeneous thyroid echotexture with the right lobe measuring 9.6×5.8×6 cm and left lobe measures approximately 9.5×8×8 cm. The thyroid function tests were normal and the FNAC was suggestive of Graves' disease. Because of the rapid progression in size and the progressive dyspnea, the patient was undertaken for a total thyroidectomy. The patient started developing symptoms of hypocalcemia on the fourth post operative day, and despite being initially started on oral calcium (1 gm TID) she did not have any improvement and was hence shifted over to IV calcium gluconate. After 4 days of IV calcium gluconate infusion (3 gm/per day) the patient was slowly shifted back to oral calcium and discharged on a dose of 2 gm per day.



Figure 2: Shows the patient with Graves disease.

Case 4

A 37-year-old man presented to the ENT department with a history of an enlarging right sided neck mass. He was drowsy, looked exhausted and weak. He had a history of left sided fracture of the hip (due to mild trauma) 1 year ago, for which he was treated. Around 5 months ago, he started having severe pain in the right thigh as well, which aggravated on walking or moving. He was being treated for the pain when suddenly within a few days, he suffered from fracture of the right femur. X-ray revealed multiple osteolytic lesions indicating secondary pathology. While being worked for the primary pathology, he presented with bilateral renal calculi (around 4 months ago) for which he simultaneously underwent treatment.

He was referred to the ENT Department in view of an elevated PTH level of 1102.98 pg/ml (normal-12-88 pg/ml), and an enlarging neck swelling. Ultrasonography of the neck showed a 2×2.3 cm² hypoechoic lesion with lobulated margins, and solid contents with vascularity in the right lobe of thyroid. Thyroid profile, and kidney function tests of the patient were normal. A CT scan and Technetium 99 MIBI scan was done to confirm the pathology, which showed persistent uptake in the right lobe of thyroid (Figure 3). A provisional diagnosis of parathyroid adenoma was arrived at, and the patient underwent right hemithyroidectomy with parathyroidectomy under general anaesthesia. The right lobe of the thyroid was also removed as there seemed to be no clear demarcation between the parathyroid and thyroid lobes, with the parathyroid seeming intrathyroidal. Post operative histopathology confirmed the diagnosis of a parathyroid adenoma.

He developed tingling and perioral numbness the very next day. Trousseau sign was found to be positive. He was initially started on 2gm of oral calcium, which was increased to 4gm oral and 2 gm IV on the fourth post operative day. IV calcium was stopped after 1 week and by the third week post operatively, the serum calcium level had stabilized and the patient was weaned off calcium supplements.

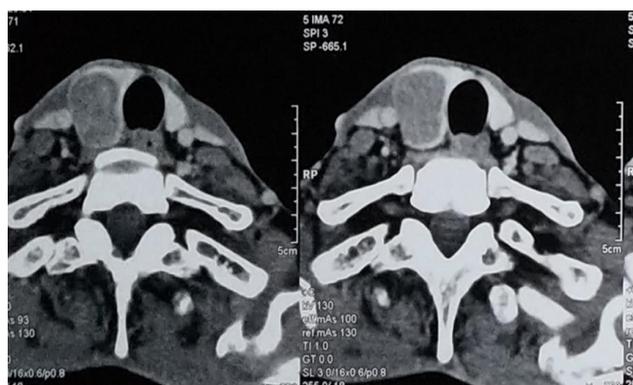


Figure 3: One of the CT images showing parathyroid adenoma.

Case 5

A 53-year-old female presented to our ENT OPD with a history of a thyroid swelling in the neck that had been operated on 6 months ago. The patient had not gone back for follow up to the doctor with her post operative histopathology report, but complained of a recurrence in the neck swelling. Her previous discharge summary showed that she had undergone a right hemithyroidectomy for a BETHESDA IV lesion, and the post operative histopathology showed a papillary carcinoma of the thyroid. Currently she said that her neck had started swelling up again in the last 2 months, with a small palpable nodule. USG showed a 2×2 cm suspicious nodule in the left lobe, and an FNAC showed a BETHESDA V nodule. A completion thyroidectomy was done and the patient started developing symptoms of hypoparathyroidism on day 2, which was treated with 1 week of or calcium supplements.

DISCUSSION

The normal range of blood calcium is typically between 2.1-2.6 mmol/L (8.8-10.7 mg/dL, 4.3-5.2 mEq/L) while levels less than 2.12 mmol/L are defined as hypocalcemia.³

Symptoms of hypocalcemia most commonly include paresthesia, muscle spasms, cramps, tetany, circumoral numbness, and seizures. Causes for the hypocalcaemic include iatrogenic hypoparathyroidism, vit D deficiency, kidney failure, pancreatitis, calcium channel blocker overdose, rhabdomyolysis, tumour lysis syndrome, and the medications such as bisphosphonates or denosumab.

Post operative hypocalcemia is the most common complication of total thyroidectomy, with an incidence varying from 30-60%, while permanent hypoparathyroidism is the most common long-term complication of the same (0-3%). It usually occurs in first few days after surgery. It can occur due to injury, devascularization, or excision of the parathyroids during surgery. Even after utmost care, it may be difficult to identify the parathyroids intraoperatively, as it can be mistaken for thyroid, adipose or nodal tissue. Such cases when undergoing total thyroidectomy run the risk of permanent hypoparathyroidism post operatively, especially if the parathyroid gland is subcapsular.⁵

In cases of malignancy of thyroid, which warrant complete removal of the gland, central compartment neck dissection is an independent risk factor for inadvertent parathyroidectomy, and the incidence is higher in such cases (up to 63% in some cases). Even in cases without neck dissection, malignancy (especially papillary carcinomas >10 mm) has shown to have a higher rate of parathyroidectomy. In some studies, up to 10% patients have developed permanent hypoparathyroidism. This can occur due to the glands being intra thyroid, malignant

invasion of glands causing firm adherence to the thyroid tissue, or due to loss of the fine boundaries between the lymph node compartment. Either way it may cause the parathyroids to either not be identified, or to be sacrificed after identification. This is the 1st situation that we have tried to highlight here.⁶⁻⁹

Additionally, in cases requiring completion thyroidectomy after primary thyroid surgery, there is a higher risk of injury to the parathyroid glands. This is due to distorted anatomy inflammation, bleeding, friability of tissues, adhesion and scar tissue, all of which make identification of the vascular pedicle difficult. A multivariate analysis by Thomusch et al showed that even in benign cases, recurrent goitre leads to a higher risk of hypoparathyroidism for the same reason.^{10,11}

The next case that we have tried to highlight here is a case of multinodular goitre. A review of literature by Agarwal et al comparing the post operative complications for patients undergoing total or near total thyroidectomy for multinodular goitre found that the rates of permanent hypoparathyroidism varied from 0-10.5% in 25 studies. This is decidedly higher than the 0-3% as stated by the 2018 American thyroid association statement on postoperative hypoparathyroidism. In fact, one of the studies with the highest levels of evidence (level II) quoted by Agarwal et al showed had the highest (10.5%) rate of permanent hypoparathyroidism. In multinodular goitre, unintentional parathyroidectomy may occur because the gland may be located intrathyroid where unintentional parathyroidectomy may range from 20-50%, or a small parathyroid may extend over the thyroid parenchyma with a thick inflammatory capsule, or the gland may be present between nodular extensions of the thyroid and may not be identified. Hence so circumvent this problem, a few studies have started advocating near total thyroidectomy in place of total thyroidectomy in multinodular goitre as they believe saving a slice of tissue near the Berry's ligament will prevent injury to the recurrent laryngeal nerve, and preserve the integrity of the upper parathyroids.¹²⁻¹⁶

Though not the same, a very similar situation is found in cases of Grave's disease. Studies have shown that the initial pathology of the thyroid does affect the post operative outcome with regards to hypoparathyroidism, with autoimmune or inflammatory diseases like Grave's and Hashimoto having a higher risk. This can be correlated to the fact that in thyrotoxicosis cases, the gland is larger and more vascular, leading to a more challenging surgery.^{10,17,18}

Finally, in cases of parathyroid adenomas, removal of the parathyroid, along with the thyroid may lead to what is known as "hungry bone syndrome" where the body, being accustomed to higher level of parathyroid hormonal, sees a rapid, intense, prolonged hypocalcemia after the removal of the adenoma, with or without removal of the concurrent lobe of thyroid. Long standing

hyperparathyroidism as in parathyroid adenoma leads to high bone turnover and extensive remodeling thus leading to increased calcium and phosphate in circulation. After removal of parathyroid adenoma there is a sudden drop of parathyroid in the circulation leading to decrease release in both calcium and phosphate from the bones. With the decline in PTH levels, osteoblastic activity becomes more pronounced, leading to increased uptake of calcium and phosphate into bones. This leads to hypocalcemia.

Surgeons should anticipate post operative hypocalcemia in patients by analyzing the predictors of hypocalcemia. Before surgery, serum calcium and PTH levels, vitamin D concentrations, and alkaline phosphatase levels should be measured and adjustments made, with calcium and vitamin D supplements. Postoperative calcium and PTH levels should be monitored in these patients. Low levels of calcium and PTH are often, predictors of postoperative hypocalcemia.¹⁹

Indocyanine green fluorescence angiography has recently been used to assess blood perfusion in the parathyroid glands. Studies have shown that this prevents postoperative hypocalcemia by ensuring at least one well-perfused parathyroid gland. This has removed the necessity to measure PTH and calcium levels intraoperatively and has provided an alternative method to measure hypoparathyroidism immediately after thyroidectomy.¹⁹ Lang et al have even developed a system to measure the quantitative value of the perfusion of the parathyroid.²⁰

Microscopic thyroidectomy is another tool that is often underutilized in thyroid surgeries, often in favour of endoscopic or robotic surgeries. But in cases of large thyroid glands, identification of landmarks and preservation of important structures is easier achieved under magnification. This is because not only the arterial supply, but damage to venous the venous outflow can result in transient hypocalcemia. More importantly the microscope is the perfect learning toll for budding surgeons to accurately identify landmarks and tackle situations like those mentioned above, where the preservation of the parathyroid gland can pose a significant challenge.^{21,22}

Most anatomical markers during thyroid surgery such as the Behr's Triangle, Joll's Triangle or Simon's Triangle are aimed at identifying the recurrent laryngeal nerve, and apart from the previously mentioned fluorescence angiography mentioned above, other intraoperative monitoring methods such as the near-infrared autofluorescence (NIRAF) imaging system or intraoperative parathyroid hormone (IOPH) although sensitive are not economically viable in a day-to-day setting.²³⁻²⁵ Hence in a setting where anatomical markers such as the course of the plane of the inferior thyroid artery, or the tubercle of Zukerkandl is distorted, as in the

cases we have shown above, it is even more imperative to keep a lookout for the parathyroids.

CONCLUSION

Thyroidectomy is a relatively safe surgery with few complications when performed by a skilled surgeon. Through this case series we have tried to highlight some of the risk factors one may face during surgery that may lead to iatrogenic temporary or permanent hypocalcemia due to inadvertent injury to the parathyroids during surgery. Not only because their appearance may be mistaken for either adipose tissue or lymph node, their position may also be variable. Additionally, there may be multiple reasons for the normal anatomical markers to get distorted, or cases where removal of the parathyroid becomes necessary. Hence in cases such as the ones discussed above, extra precaution should be taken to try and identify and preserve at least one parathyroid gland to prevent lifelong morbidity due to hypocalcemia. Careful dissection, tracing of the blood supply via inferior thyroid artery and ligation of the artery beyond its branching point should be stressed upon. Additionally, one must be on the lookout for such challenging cases preoperatively and appropriate consent should be taken from the patient beforehand.

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