Potential protection of indocyanine green on parathyroid gland function during near-infrared laparoscopic-assisted thyroidectomy: A case report and literature review

Shu-Jia Peng, Ping Yang, Yan-Ming Dong, Lin Yang, Zhen-Yu Yang, Xi-E Hu, Guo-Qiang Bao

Shu-Jia Peng, Ping Yang, Yan-Ming Dong, Lin Yang, Zhen-Yu Yang, Xi-E Hu, Guo-Qiang Bao, Department of General Surgery, Tangdu Hospital, Air Force Military Medical University, Xi’an 710032, Shannxi Province, China

Corresponding author: Guo-Qiang Bao, MD, Assistant Professor, Associate Chief Physician, Doctor, Surgeon, Department of General Surgery, Tangdu Hospital, Air Force Military Medical University, No. 569 Xinsi Road, Xi’an 710032, Shannxi Province, China. guoqiang@fmmu.edu.cn

Abstract

BACKGROUND
In recent decades, significant advances have been made in protecting the parathyroid glands and recurrent laryngeal nerves during thyroidectomy. However, reliable and convenient technical means are still lacking. In this study, the reliability, safety and feasibility of near-infrared (NIR) laparoscopy-assisted thyroid lobectomy with isthmectomy and prophylactic central lymph node dissection (CLND) were reported.

CASE SUMMARY
A 63-year-old female patient with a free previous medical history, was admitted to our department due to multiple thyroid nodules. Ultrasonic examination suggested diffuse thyroid changes and one thyroid nodule in the right upper lobe with the largest diameter of 1.5 cm adjacent to the trachea and Breast Imaging Reporting and Data System grade 4B. Imaging examination of the neck showed no obvious enlarged lymph nodes. Fine needle aspiration biopsy suggested a papillary thyroid carcinoma. Combined with thyroid function examination, the patient was diagnosed with papillary thyroid carcinoma and Hashimoto’s thyroiditis. Considering the risk of invading the capsule and the patient’s extreme anxiety, a right thyroid lobectomy with isthmectomy and prophylactic central lymph node dissection (CLND) was planned. No significant abnormalities were found during preoperative examinations, except for an increased thyroid stimulating hormone level. The patient underwent NIR laparoscopy-assisted thyroid lobectomy with isthmectomy and prophylactic CLND. During the operation, two right parathyroid glands (PGs) adjacent to the thyroid gland capsule and the right recurrent laryngeal nerve (RLN) were examined by indocyanine green (ICG) fluorescence using a NIR fluorescence camera, and the PGs and RLN were...
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INTRODUCTION
Differentiated thyroid cancer, which includes papillary and follicular cancer, is becoming increasingly prevalent[6]. The incidence of thyroid cancer is increasing partly due to improved diagnostic methods such as ultrasound and other imaging methods, and the early detection of small papillary thyroid carcinomas (PTCs)[3, 4]. There is no consensus on the surgical indications and surgical methods for PTCs. However, surgery is the optimum treatment for PTCs with high-risk factors. In addition, many patients choose surgical treatment due to fear and the inconvenience of follow-up. According to current practice and various guidelines, hemithyroidectomy is recommended for a tumor less than 4 cm and minor extrathyroidal extension (T2 stage)[3]. Prophylactic central lymph node dissection (CLND) may reduce lymph node (LN) recurrences, and the probability of reoperation[7]. With strict control of surgical indications and contraindications, endoscopic surgery is safe and feasible in selected patients[8]. Injury to the parathyroid glands (PGs) and recurrent laryngeal nerve (RLN) are the main postoperative complications of thyroidectomy. Due to their small size and close proximity to thyroid tissue, even though with clear anatomical background and careful dissection, it is hard to avoid inadvertent injury to the PGs. Disruption of parathyroid vasculature, direct trauma, or removal of PGs may result in symptomatic hypoparathyroidism and hypocalcemia[9, 10]. A retrospective analysis of patients who underwent minimally invasive video-assisted thyroidectomy showed that the occurrence rate of transient hypoparathyroidism was 7% and definitive hypoparathyroidism was 0.4%[11]. The basis of parathyroid preservation in thyroid surgery is the identification of as many PGs as possible. Thus, accurate identification of PGs could reduce the risk of complications and influence management strategies. Several techniques, such as the use of intravenous methylene blue, indocyanine green (ICG), carbon nanoparticles (CNs), and colloidal gold immunochromatography, have been developed to aid in the identification of PGs[12]. In recent years, near-infrared...
(NIR) fluorescence imaging with ICG has become a useful tool to identify and preserve PGs. ICG fluorescence imaging is a simple, rapid and repeatable method capable of visualizing and assessing the function of PGs intraoperatively\[13\]. Besides standard endoscopic magnification using video-assisted approach, enhanced visualization of parathyroid tissue can be confirmed by NIR. Furthermore, ICG injection was used to confirm the vascular supply of preserved PGs at the end of the operation\[14\]. In recent decades, significant advances have been made in protecting PGs and RLNs during thyroidectomy. However, reliable and convenient technical means are still lacking.

In this study, the reliability, safety, and feasibility of NIR laparoscopy-assisted thyroid lobectomy with isthmectomy and prophylactic CLND were reported.

CASE PRESENTATION

Chief complaints
A 63-year-old woman was admitted to our department due to multiple thyroid nodules.

History of present illness
The patient had no discomfort. Imaging examination of the neck showed no obvious enlarged LNs. Fine needle aspiration biopsy suggested PTC.

History of past illness
The patient had no history of other diseases.

Physical examination
On admission, her body temperature was 36.2°C, heart rate was 87 bpm, breathing rate was 16 breaths/min, blood pressure was 128/76 mmHg, and room air oxygen saturation was 99%. A 1.5 cm sized hard nodule in the left neck was palpated, with a clear boundary and irregular shape, moving up and down with swallowing, and no obvious enlarged LNs were found. Other physical examinations showed no obvious abnormalities.

Laboratory examinations
No significant abnormalities were found during preoperative examinations, except for an increased thyroid stimulating hormone (= 6.8, reference range: 0.27-4.2 μIU/mL) level. The level of parathyroid hormone was 52.3 pg/mL (reference range: 15-65 pg/mL), the level of Ca\(^{2+}\) was 2.55 mmol/L (reference range: 2.10-2.90 mmol/L), respectively.

Imaging examinations
Ultrasonic examination (The Endocrine Clinic, Singapore), suggested diffuse thyroid changes and one thyroid nodule in the right upper lobe with the largest diameter of 1.5 cm adjacent to the trachea and Breast Imaging Reporting and Data System grade 4B.

FINAL DIAGNOSIS

PTC and Hashimoto’s thyroiditis.

TREATMENT

Considering the risk of invading the capsule and the patient’s extreme anxiety, a right thyroid lobectomy with isthmectomy and prophylactic CLND was planned. Thyroid surgery was performed by three experienced surgeons. The surgical technique was based on a previously described procedure with slight modifications\[15\]. ICG (0.5 mg/kg) was intravenously administered 1 h before initiation of anesthesia after confirmation that the patient was not allergic to ICG. Under general anesthesia, the patient was placed in the supine position with her head hyperextended. A 10 mm incision was made on the superficial layer of the subcutaneous fascia of the anterior chest wall at the level of the nipple. About 50 mL normal saline and adrenaline
Surgery is the basic treatment for PTC. Generally, nodules > 1 cm are potentially clinically significant cancers. Some nodules < 1 cm should also be evaluated due to presence of clinical symptom or swollen LNs. Many established guidelines advise doctors to avoid overtreatment in a majority of patients at low risk, while high-risk patients should be appropriately monitored and managed\(^{[86]}\). For small PTCs, previous studies have reported that patients who underwent total thyroidectomy had better prognosis than those who received other therapies\(^{[7]}\), including low-risk patients. However, lobectomy did not increase the loco-regional recurrence risk of the contralateral remnant lobe. As total thyroidectomy can safely manage recurrence of the contralateral remnant lobe, it is a safe option for selected patients with small PTCs\(^{[86]}\). In China, more patients with PTC choose surgical treatment. The extent of surgery for PTC significantly differs in different medical centers and by different surgeons. For low-risk patients, the more limited thyroidectomies, e.g., lobectomy with isthmectomy, have been adopted, although prophylactic LN dissection has been performed. Although patients with T1N0M0 have an excellent prognosis following thyroidectomy without radioiodine therapy, hemithyroidectomy is adequate if a 1% risk of recurrence of the remnant thyroid is acceptable\(^{[80]}\). Morbidity due to PTC is mostly derived from LN metastasis, which lead to reoperations and complications associated with these surgeries. Ultrasound is not the best method for determination of LN metastasis and routine central node dissection. Prophylactic CLND appears to reduce LN recurrences, and the probability of reoperation\(^{[8]}\). In a study, 96% of patients underwent prophylactic CLND, pathological examination showed positive LNs in 57% of patients. Many studies suggested that the sentinel node biopsy with removal of other LNs belonging to the sentinel node compartment, is a safe procedure\(^{[83]}\). In our
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Figure 1 The procedure for near-infrared endoscopy-assisted right thyroid lobectomy with isthmectomy and prophylactic central lymph node dissection. A: Creating the operative space; B: Exposing the thyroid lobe (modified detachable retractor, orange arrow) in near-infrared (NIR) mode; C: Investigating the parathyroid gland (PG) in NIR mode (PG, orange arrow); D: Exposing the right recurrent laryngeal nerve (RLN) in NIR mode (RLN, orange arrow); E: Performing central lymph node dissection under the guidance of fluorescence imaging in NIR mode (PG, orange arrow); F: Excising the lymphatic tissue and soft tissue surrounding the RLN in NIR mode (RLN, orange arrow); G: The final operative field in NIR mode; H: The final operative field in white light mode. PT: Papillary thyroid; RLN: Recurrent laryngeal nerve; CCA: Common carotid artery.

department, we usually perform limited lobectomy with isthmectomy + prophylactic CLND for patients with low-risk single small PTC. Hypoparathyroidism, an ongoing and frequently underestimated complication after thyroid operation, leads to hypocalcemia and serious medical problems[26,27]. Comparing hemithyroidectomy with all other surgical procedures, prolonged surgery (total thyroidectomy) and the diagnosis of malignancy are predictors of transient and permanent hypoparathyroidism[28]. Careful separation by an experienced surgeon using capsule separation techniques can reduce the incidence. In addition, CLND is reported to be the most frequent risk factor of incidental parathyroidectomy[29]. Incidental parathyroidectomy is considered a minor finding in final histopathology, but it is important for the thyroid surgeon to be able to identify the factors that increase the risk of incidental parathyroidectomy during thyroidectomy and exercise appropriate caution in these patients[30]. Despite the risk of unavoidable incidental parathyroidectomy, careful dissection and meticulous intraoperative identification of PGs can reduce the incidence of incidental parathyroidectomy[31]. Although preservation of the surrounding vasculature and capsule dissection techniques are used to avoid incidental parathyroidectomy or disruption of the parathyroid vasculature, reliable tools to both identify and assess PGs during surgery, and to predict whether a patient will develop hypoparathyroidism, are limited[32]. In China, CNs have been widely used for the intraoperative identification of the sentinel LN in various cancers, which shows the highest detection rate and accuracy[32-34]. CNs have also been used to identify the PGs and trace the LNs in the initial surgery for thyroid cancer in recent years[31]. CNs application markedly improves LN detection rate and decreases the rate of incidental parathyroidectomy, which potentially improves the management of PTC patients[31]. CNs significantly decrease the incidence of permanent and transient hypoparathyroidism and reduce the mean recovery time for transient hypoparathyroidism, thus improving the postoperative quality of life of patients[31,32]. Recent studies have demonstrated the feasibility and effectiveness of ICG in thyroid surgery. NIR fluorescence imaging with intravenous ICG has been used for the identification of PGs during thyroid and parathyroid surgery. It can provide certainty on the location of PGs, especially to confirm the presence of a suspect PG. Intraoperative ICG fluorescence imaging is a simple, fast and reproducible method capable of visualizing and assessing the function of PGs intraoperatively[33,34]. Angiography with ICG has been performed in patients undergoing thyroid surgery, to visualize vascularization of identified PGs. ICG imaging during total thyroidectomy is feasible. ICG might be a useful adjunct to the identification of patients with hypothyroidism after thyroidectomy[35]. In a study that included 36 patients, at least one well vascularized PG was demonstrated by ICG angiography in 30 patients, and PTH levels on POD 1 were normal in all these patients, and none required treatment for hypoparathyroidism[34]. Three branches arise from the superior border of the aortic arch: The left subclavian artery, the left common carotid artery, and the brachiocephalic trunk. The brachiocephalic trunk divides into the right common carotid artery and the right subclavian artery. This branching type was first classified
as the normal pattern type A by the anatomist Buntaro Adachi (1865-1945) in 1928[9]. In this case, the right common carotid artery straddled the trachea. This variation is seen in about 1% of patients in our clinical practice. To some extent, this variation facilitates CLND in endoscopic thyroidectomy. In the present patient, NIR endoscopy was used for lobectomy with isthmectomy + prophylactic CLND. ICG fluorescence was helpful in the identification and protection of PGs. In NIR mode, the color difference between the PGs and the surrounding background effectively prevented incidental parathyroidectomy following CLND. In addition, since there is no fluorescence imaging of the RLN, the display is more obvious under the magnification of the endoscope, which may be beneficial in the protection of RLN function.

CONCLUSION

In endoscopic thyroid surgery, NIR fluorescence endoscopy can be selected, which, combined with ICG, may contribute to functional protection in thyroid surgery. Of course, the application value of NIR endoscopy in thyroid surgery needs to be further studied and discussed.

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