

Implantation of cancer cells from transoral endoscopic thyroidectomy: a case report

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Background: With the development and new technological knowledge, such as surgical techniques that accompany the consolidated open surgical procedures, minimally invasive strategies have also emerged for thyroid surgery. Among these, we can cite the transoral endoscopic vestibular approach known as TOETVA. Recurrences and metastases of differentiated thyroid cancer frequently manifest in the lymph nodes, lungs, bones, and liver. Although the primary implantation of cancer cells causing these recurrences and metastases is considered an uncommon event, it can nonetheless occur in specific instances. This can be a serious complication for patients, as these recurrences and metastases can be difficult to detect and treat effectively. Early identification and appropriate management of these cases are crucial for improving patient outcomes.

Case Description: We present a case of a 55-year-old male patient with recurring muscular and subcutaneous recurrence that developed five years after the initial left thyroidectomy performed via a TOETVA. The patient therefore required a second surgical procedure of completion thyroidectomy, central lymph node dissection (level 6 and 7), and removal of nodes in subcutaneous tissue and muscle.

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Conclusions: Tumor biology, local environment, technical issues, surgical skills, and the correct management and handling of neoplastic nodules represent crucial clinical pitfalls and important factors that can contribute to local recurrence and malignant cellular implantation following a TOETVA for thyroid surgery.

Keywords: Thyroid cancer (TC); transoral thyroid surgery; metastases; transoral endoscopic vestibular approach (TOETVA); case report

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Introduction

The most common sites for recurrence and metastasis of differentiated thyroid cancer (TC) are the regional lymph nodes, as well as distant sites such as the lungs, bones, and liver (1,2). While differentiated TC generally carries an excellent prognosis, the development of metastatic disease significantly impacts patient management and long-term outcomes. The propensity for these specific sites stems from the tumor's biological characteristics and vascular dissemination patterns. However, the implantation of cancer cells leading to recurrence and metastasis in unusual locations, such as muscular and subcutaneous tissues, is rare and often represents a more aggressive disease phenotype (*Table 1*) (3-8). The incidence of muscular, subcutaneous, and skin metastases from differentiated TC is reported to be between 0.8% and 1.0% (1-9). These atypical metastases, particularly in muscular and subcutaneous sites from TC, are generally associated with a notably poor prognosis,

reflecting advanced disease and a greater challenge for effective treatment (9-11).

We present the case of a 55-year-old man who underwent thyroidectomy via a transoral endoscopic vestibular approach (TOETVA) and subsequently experienced a recurrence of muscular and subcutaneous tissue from TC. This recurrence was treated through local resection and revision surgery. We present this article in accordance with the CARE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-2025-85/rc>).

Case presentation

A 55-year-old male patient, without any significant clinical history or family history positive for thyroid disease, underwent medical evaluation in 2016 because of swelling in the neck and ultrasound findings of a homogeneous isoechoic thyroid nodule on the left, sized 37 mm × 26 mm. Fine-needle aspiration (FNA) revealed that the nodule was a benign lesion, categorized as a category II thyroid lesion (Bethesda System for Reporting Thyroid Cytopathology) (10). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki and its subsequent amendments. Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

The patient underwent left TOETVA under general anesthesia. The intervention was carried out by a specialized team with proven skills and extensive certified experience in thyroid surgery. The intervention was performed using the TOETVA technique as standardly described in the literature (11-16). The patient was positioned on the operating table in a supine position with slight neck

Highlight box

Key findings

- We evaluated recurrence and metastasis of differentiated thyroid cancer (TC), especially after mini-invasive approach for thyroid neoplasms.

What is known and what is new?

- Differentiated TC commonly metastasizes to lymph nodes, lungs, bones, and liver.
- Muscular, subcutaneous, and skin metastases are rare. Unfortunately, seeding of cancer cells may occur at the sites of ports of endoscopic instruments.

What is the implication, and what should change now?

- Understanding the role of tumor biology, local microenvironment, and applying advanced surgical techniques will become crucial to prevent tumor cell seeding.

Table 1 Neoplastic implantation after thyroid procedures

Author, year	Cases	Type of procedure	Tumor pathology, dimensions, stage	Bag specimen retrieval	Tumor fragmentation	Location	Interval (months)	Treatment	Follow-up (months)
Sevinç AI, 2010 (3)	1	FNA biopsy	PTC	–	–	Skin, muscle	4	Local excision; total thyroidectomy; RAI	–
Dong X, 2020 (4)	1	Open conventional thyroidectomy	FPTC; 25 mm; N0	Yes	No	Subcutaneous	60	Local excision; RAI	–
Espiard S, 2015 (5)	2	Transaxillary thyroidectomy	PTC; 30 & 40 mm; N0	Yes	No	Subcutaneous	18 & 36	Local excision; RAI	–
Li S, 2012 (6)	1	Areola thyroidectomy	PTC; 30 mm	Yes	No	Subcutaneous, muscle	12	Local excision; RAI	–
Laohathai S, 2024 (7)	1	TOETVA	Benign nodular goiter; 31 mm	Yes	No	Subcutaneous	48	Local excision	–
Oh MY, 2024 (8)	1	TOETVA	FTC; 30 mm	Yes	Yes	Subcutaneous	27	Local excision; total thyroidectomy; RAI	–
Our report	1	TOETVA	Non-invasive capsulated follicular variant of papillary carcinoma	Yes	No	Subcutaneous, muscle	78	Local excision; revision surgery; RAI	Alive, no recurrence +18 months

FNA, fine-needle aspiration; FPTC, follicular variant PTC; FTC, follicular thyroid cancer; PTC, papillary thyroid cancer; RAI, radioactive iodine therapy; TOETVA, transoral endoscopic vestibular approach.

extension and underwent endotracheal intubation. The surgical field was thoroughly disinfected with an antiseptic alcohol solution. Three small incisions were made in the mucosa of the inferior oral vestibule: one central incision and two lateral ones. Through these incisions, operative trocars were inserted. By insufflating carbon dioxide at low pressure (6 mmHg), a stable working space was created anterior to the thyroid gland, so that the insertion of a 30° endoscope through the central trocar provided a magnified and illuminated view of the surgical field. Dedicated instruments were inserted through the lateral trocars. Under direct endoscopic vision, the subcutaneous planes were dissected, creating a tunnel from the mouth to the neck. Laryngeal nerve structures were identified and preserved through intraoperative neurophysiological monitoring to localize them and test their functionality in real-time. The left thyroid lobe was mobilized and separated from the trachea, followed by sectioning of the isthmus and sectioning of the thyroid vessels with an ultrasound device. The working space was carefully inspected to ensure hemostasis. The vestibular incisions were closed with

absorbable sutures. The initial TOETVA procedure was noted to be technically challenging due to the size of the nodule. This required significant manipulation to mobilize the lobe within the confined working space. However, despite the described technical difficulty, no deviation from the normal operative procedure was observed. During the procedure, no fragmentation of the specimen occurred. The neoplasm was removed through the vestibular incision through a protective retrieval bag and then sent for pathologic examination.

The final pathology documented nodular, encapsulated proliferation with a completely follicular architecture of the thyrocytes and nuclear features of papillary thyroid carcinoma (PTC). There was no evidence of capsular and vascular invasion, no necrosis, and a mitotic index less than 1 per 10 high-power fields (×400). Additionally, no psammomatous corpuscles were observed. The histologic picture was consistent with a noninvasive capsular-follicular variant of PTC, which has recently been reclassified as a noninvasive follicular thyroid neoplasm with papillary nuclear features (17). After surgery, the

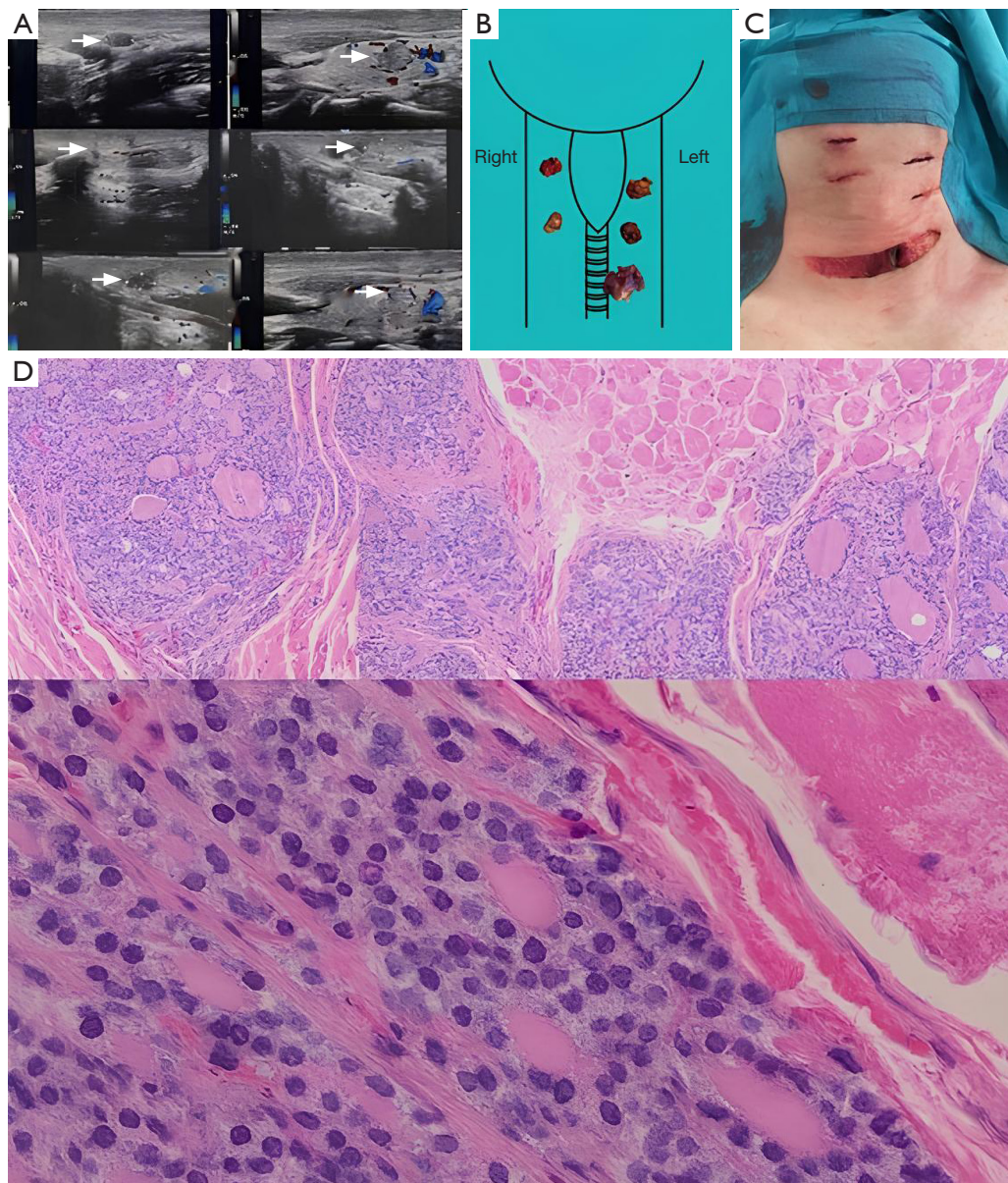


Figure 1 Recurrence and pathological findings following TOETVA. (A) Sonographic image of recurrent nodules in subcutaneous tissue and muscle (white arrows indicate the nodules). (B) Schematic showing cancer cell implantation during TOETVA and overall view of resected nodules. (C) Postoperative photograph indicating linear surgical seeding. (D) Pathologic section showing follicular variant of PTC infiltrating fibroadipose tissue and striated muscle (H&E staining; magnification $\times 10$, $\times 40$). H&E, Hematoxylin & Eosin; PTC, papillary thyroid cancer; TOETVA, transoral endoscopic vestibular approach.

patient was followed up regularly. No L-tiroxine therapy was administered. In March 2021, a sonogram of the patient's neck revealed the presence of subcutaneous and muscular hypoechoic nodules (*Figure 1A*). A left paratracheal isoechoic nodule measuring 7 mm \times 17 mm \times 14 mm was present. The remaining right lobe showed no

distinct nodules. No suspicious lymph nodes were detected in the lateral compartment. FNA of the left paratracheal nodule had atypia of undetermined significance-category III (8). Laboratory tests focused on thyroid function showed the following results: thyroid-stimulating hormone (TSH) 1.14 mIU/mL, thyroglobulin antibodies

(AbTg) <15 U/mL, thyroglobulin (Tg) 6.4 mcg/L. The patient then underwent secondary surgery. A complete thyroidectomy, central lymph node dissection (level 6 and 7), and removal of nodes in subcutaneous tissue and muscle were performed under general anesthesia (*Figure 1B,1C*). Pathologic examination of the resected specimen revealed that all nodules contained PTC tissue (*Figure 1D*). Lymph node metastases were not detected during the evaluation. Following the second surgical procedure, the patient recovered well and experienced an uneventful postoperative course. The patient received radioiodine treatment and TSH suppression treatment with levothyroxine.

Discussion

In the past 5 years, TOETVA has been accepted by surgeons and patients because of its excellent cosmetic effect (11-16). However, there are still some limitations (*Table 2*) (15,16,18-30).

Here, we report an unfavorable case, a man in whom subcutaneous and muscular metastases were implanted following the path of the endoscopic instruments. The linear surgical approach, the working channel of the endoscopic instrumentation and the location of the metastases indicated that the seeding was certainly from TOETVA (*Figure 1*). To our knowledge, this is the first case of TC implantation of cancer cells from TOETVA. Local implantation after endoscopic surgery for thyroid disease is considered a complication (6).

Implantation of tumor cells is not a new phenomenon (*Table 1*). Authors have reported cutaneous, subcutaneous, and muscular recurrences after FNA, open surgery, transaxillary, and areolar endoscopic approaches (3-6). The exact incidence of tumor implantation metastases after endoscopic thyroid surgery is not assessable until the denominator of this number of procedures is known. However, not every endoscopy procedure is associated with insertion site metastases in the literature. There are no known cases of TC implants after minimally invasive video-assisted thyroidectomy (MIVAT), even after retroauricular access. It is difficult to draw any conclusions, but it at least confirms the consistency of MIVAT, which has been present in the scene of endoscopic thyroid surgery for at least 23 years (31).

The indications for TOETVA have been expanded from benign thyroid disease to small differentiated and non-metastatic TC (16). The oncologic safety of TOETVA in malignancies has been analyzed (12,15,30). A recent analysis examined the short-term outcomes

of 100 PTC patients treated with TOETVA. This is currently the largest series of TC treated with TOETVA. The average tumor size was 0.8 ± 0.5 cm. Nine patients underwent total thyroidectomy and 91 underwent lobectomy. Ipsilateral prophylactic central compartment dissection was routinely performed, with 5.0 ± 3.6 lymph nodes harvested. Cervical lymph node metastasis was detected in 34 patients. Seventy-eight cases were papillary microcarcinoma and 22 were papillary carcinoma. A total of 77 patients were at stage I and 23 patients were at stage II. No cases of local recurrence or tumor implantation were described during the short follow-up period (median 16.1 months; range 8.2–20.4 months) (21). The excellent results of this study are certainly due to the precise criteria for patient selection and perhaps also to the optimal robotic manipulation of the thyroid nodule and lymph nodes (32).

Although implantation after endoscopic surgery is uncommon, our case reminds us to offer TOETVA to TC with caution. Moreover, tumor seeding after endoscopic oncologic surgery is rare and does not appear to be greater than what has been reported in the past for open thyroid surgery (4). Strict indications for endoscopic surgery, comprehensive preoperative evaluation, careful intraoperative management, and effective protective measures can reduce the incidence of locoregional implantation or recurrence. In our experience, TC should be candidates for TOETVA who have an estimated ultrasonography (US) major nodal size <20 mm, TC without extrathyroidal extension, TC without evidence of central lymph node metastasis, recurrent laryngeal nerve (RLN) palsy, TC without concurrent Graves' disease, or a US estimated thyroid volume >40 mL (16).

The pathogenesis of tumor cell implantation in TOETVA can be explained in several ways. (I) Tumor-related: the biological aggressiveness of the tumor, as represented by the high grade and high stage, could play a crucial role in determining the possibility of tumor seeding. Proper preoperative criteria for patient selection and cautious intraoperative evaluation will minimize tumor implantation in the future. (II) Local immune response: altered immune response could be an adverse event contributing to the rare development of tumor seeding. Further studies are needed to explore the immune response during TOETVA. (III) Operative: tumor implantation may result from tumor spillage during excessive tumor manipulation, instrument contamination, tumor cell aerosolization, chimney effect, surgical technique, and

Table 2 A note of caution: TOETVA specific drawbacks and complications. Null mortality is reported from the literature

First author, year	Drawback	Preventive maneuver
Our report	Implantation of cancer cells (subcutaneous and muscle)	Awareness that some patients may develop TC implantation Patient selection instances [†]
Zhang D, 2021 (18)	Applying the IONM trouble-shooting algorithm	Different modes of IONM are available: long stimulators, percutaneous, and adapted to the surgical dissector
Zhang D, 2020 (19); Anuwong A, 2018 (16)	Mental nerve injury	Vestibular lateral incisions carried more external, lateral, near the border of the lip Careful tunneling for trocar insertion
Zhang D, 2019 (20)	Different range of interpretations of pain between TOETVA and open surgery	Pain treatment in the lip and chin
Zhang D, 2018 (21)	Pneumomediastinum	CO ₂ insufflation <6 mmHg External retractors
Zhang D, 2019 (22)	CIONM during TOETVA is not feasible	CIONM probe positioning is easier with robot
Zhang D, 2021 (23)	Cicatricial diathesis, synechia with gingiva developed in the central vestibular incision	Central vestibular incisions >10 mm from the gingiva tended not to form synechia
Long SM, 2022 (24)	Thyrohyoid membrane injury Thyroid notch to Broyle's ligament injury without avulsion	Primary repair
Karakas E, 2022 (25)	Transient increase in WBC (not associated with significant increase in WI)	Intravenous antibiotic prophylaxis, oral mucosal disinfection, and preparation of dental care
Smith SM, 2022 (26); Wu YJ, 2018 (27)	Specimens disrupted/fragmented	Additional axilla incision
Chai YJ, 2017 (15)	Zygomatic bruising	Protective sponge application over the zygoma
Anuwong A, 2018 (16)	Dimpling on the chin	Spontaneously recovers in 3–6 months
Bakkar S, 2018 (28)	Skin flap perforation	Careful axial (parallel) vestibular dissection with blunt Mosquito forceps
Kim KN, 2018 (29)	CO ₂ embolism	CO ₂ insufflation <6 mmHg External retractors
Kim HK, 2019 (30)	Oral commissure tearing	Oral mucosal protection sutures Plaster application over commissures

[†], TC candidates for TOETVA: US estimated main nodule size <20 mm, PTC without extrathyroidal extension, PTC without evidence of central lymph node metastasis, concurrent Graves' disease or US estimated thyroid volume >40 mL. CIONM, continuous intraoperative neural monitoring; PTC, papillary thyroid carcinoma; TC, thyroid cancer; TOETVA, transoral endoscopic vestibular approach; US, ultrasonography; WBC, white blood cell count; WI, wound infections.

experience (*Table 3*) (13-16,25-29,33,34). In literature, it has been recognized for decades that tumor manipulation increases tumor metastasis in both open and laparoscopic surgery. An entrapment bag should always be used for intact specimen collection, as direct contact between the surgical specimen and the wound may promote tumor seeding. The size of the vestibular incision plays a paramount role. An

incision that is too small for specimen collection may cause tissue trauma and fragmentation and may be responsible for tumor implantation. Tumor implantation is very likely when a malignant tumor is removed through a narrow vestibular incision (25,26). Another hypothesis is that CO₂ has a stimulatory effect on tumor growth. Experimental studies on rats with suspensions of colon cancer cells found

Table 3 Potential strategies for preventing tumor spillage in TOETVA. Every action made to prevent tumor spillage should be recorded in the surgical report

Preventive maneuver	References	Strategies
Patient selection	(16,25,26,29,33,34)	Low risk PTC Differentiated TC Estimated US major nodal size <20 mm Exclude PTC with extrathyroidal extension Exclude c/pN1 PTC Exclude preoperative RLN palsy Exclude concurrent Graves' disease US estimated thyroid volume <40 mL
Operative technique	(13-15,29,33,34)	Surgeon with experience in open surgery and endoscopy Enlarge size of vestibule incision during specimen removal or use additional axillary access Meticulous surgical technique Reduce excessive nodule manipulation Accurate control of hemostasis Wide dissection of neck air pocket Conversion to open surgery if fragmentation occurs Conversion to open surgery if capsule occurs Avoid isthmectomy in case of an isthmic or paraisthmic nodule Extensive dissection of the sternothyroid muscle with good exposure of the superior pedicle in the case of an apical nodule Auditing
Instrumentation	(16,25-29,33,34)	Keep CO ₂ insufflation <6 mmHg Use external retractors to limit the use of CO ₂ All surgical specimens should be extracted within a containment bag After surgery, the neck cavity is profusely washed with physiological serum Robotic surgery appears to handle nodules more delicately

PTC, papillary thyroid carcinoma; RLN, recurrent laryngeal nerve; TC, thyroid cancer; TOETVA, transoral endoscopic vestibular approach; US, ultrasonography.

that there was no tumor deposition at the trocar sites during gasless laparoscopy, whereas tumor growth was noted at the trocar sites after CO₂ insufflation. Tumor models found more metastases at the port sites after laparoscopic resection of the tumor than after open resection (34).

Conclusions

In summary, future experimental and epidemiologic research

should focus on investigating the role of tumor biology, the local tumor microenvironment, alternative surgical gases, gasless endoscopic techniques, and advanced surgical skills in both establishing and preventing the implantation of tumor cells during TOETVA (35). Traumatic handling of the thyroid nodules during the procedure and the surgeon's level of expertise appear to be the most important factors contributing to local recurrence or implantation following TOETVA.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gc-2025-85/rc>

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