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ORIGINAL ARTICLE

Extrathyroidal Implantation of Thyroid Hyperplastic/neoplastic Cells after Endoscopic Thyroid Surgery

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Key words: endoscopic thyroid surgery; benign thyroid tumor; malignant thyroid tumor; subcutaneous tissue; implantation

Objective To report a case of the implantation of thyroid hyperplastic or neoplastic tissue after endoscopic thyroidectomy and discuss this complication in aspects of prevalence, pathogenesis, protection, and therapies.

Methods A systematic search of literature from the PubMed database was conducted for identifying eligible studies on implantation of thyroid hyperplastic or neoplastic cells after endoscopic thyroid surgery.

Results Overall, 5 reported cases on patients suffering from endoscopic thyroid surgery with implantation of thyroid hyperplastic or neoplastic cells were included in the systematic review.

Conclusions Unskilled surgeons, rough intraoperative surgical treatment, scarification or rupture of tumor, contamination of instruments, chimney effect, aerosolization of tumor cells may be associated with the implantation after endoscopic thyroidectomy. To minimize the risk of such complication, we should be more meticulous and strict the endoscopic surgery indications.

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RECALLING the history of minimally invasive thyroid surgery, the measures of minimal invasive approaches to the thyroid and parathyroids were firstly described by Gagner in 1996.¹ In the following decades, endoscopic thyroidectomy was rapidly developed. Nowadays, it has not only been widely adopted by surgeons and patients for its excellent cosmetic effect, but also applied to solitary thyroid nodule, Graves' disease, multinodular goiter, low-risk differentiated thyroid cancer, and central compartment neck dissections, as demonstrated in numerous studies.²⁻⁴ However, retrospective

study shows that complications such as implantation of thyroid carcinoma after fine-needle aspiration biopsy or endoscopic thyroid surgery⁵ may occasionally occur despite the rareness of implantation of benign tumor. Hereinafter, the cases of the implantation of thyroid hyperplastic or neoplastic tissue after endoscopic thyroidectomy were reported and the complication was discussed in aspects of prevalence, pathogenesis, protection, and therapies.

PATIENTS AND METHODS

A systematic search of literature in the PubMed database was conducted in which key terms being

“endoscopic thyroid surgery”; “benign thyroid tumor”; “malignant thyroid tumor”, “subcutaneous tissue”; and “implantation”. In addition, numerous potentially eligible reports were found by manual search for reference. No language restriction was imposed. The following information was recorded: sex, size, operation, pathology, interval between surgery and implantation, number of implanted lesions, and location of implanted lesions. One case in our hospital was described.

RESULTS

Illustrative patient

Taking one typical case as an example, in which a 21-year-old female patient in our hospital (Department of General Surgery) was referred to, with a record of enlarged right thyroid nodules and growing masses in the subcutaneous soft tissue of right neck. Five years ago during her presence in another hospital, appeared on her medical records were several nodules with the maximal size of 2.2 cm×2.0 cm×2.0 cm. She underwent an endoscopic partly right hemithyroidectomy. Histopathologic diagnosis at that time was multinodular goiter. The operation procedures will be elaborated in following detail: The patient was positioned supine with one arm extended; two skin incisions were made in right axilla, while the other two were separately made in right breast and anterior chest wall; trocars (10 mm) were inserted into the incisions and carbon dioxide gas was insufflated up to 6-8 mm Hg; endoscopic scissors were used for an additional blunt and sharp dissection to enlarge the subplastysmal space; then the surgeons found numerous nodules in the right thyroid and then made partial right hemithyroidectomy.

Once the patient was admitted to our hospital, ultrasonography was immediately performed. The results showed several mixed echoic nodules with calcification in the remnant right thyroid gland with maximal size of 3.1 cm × 2.1 cm×2.0 cm (Fig. 1A); there also showed subcutaneous

iso-echoic nodules with maximal size of 1.3 cm×1.0 cm×0.7 cm in the right anterior neck (Fig. 1B) and an iso-echoic nodule in the infraclavicular fossa in size of 2.4 cm×1.0 cm×0.9 cm (Fig. 1C). The bilateral neck lymph nodes were visible while the structure of lymph node in infraclavicular fossa was disorder, which leads to suspicion of doubtfully lymph node metastasis. Laboratory data indicated that euthyroid and thyroglobulin measurement were in the normal range, and anti-thyroid microsomal and thyroglobulin antibodies were both negative. The patient underwent a secondary operation, during which several hard subcutaneous nodules with maximal diameter of 1 cm were found in the right subcutaneous fat layer and anterior cervical muscle; the right thyroid gland was nearly occupied by hard nodules with maximal size of 3.0 cm×3.5 cm ×2.0 cm. A total right hemithyroidectomy and excision of nodules in the muscle were performed. Histopathologic examination of all the nodules removed from the right thyroid and right neck confirmed the diagnosis of nodular goiter with adenomatous hyperplasia (Fig. 2). The subcutaneous nodule showed nodular goiter with adenomatous hyperplasia within fibrous connective tissue and skeletal muscle tissue; immunostaining of galectin-3 was negative (Fig. 3A) and ki-67 labeling index of subcutaneous nodules was about 3% (Fig. 3B); partial cells in the subcutaneous nodule showed active proliferation. The patient was discharged uneventfully from the hospital 7 days after the surgery.

In this case, it describes a recurrence and subcutaneous implantation of nodular goiter with adenomatous hyperplasia. The close relationship between the locations of nodules and the field of the previous surgery is highly suggestive of surgical dissemination of benign thyroid tissue. Evidently, these lesions were due to the implantation.

Retrieval results

Only six cases of the implantation of hyperplastic thyroid tissue after endoscopic thyroidectomy were enrolled in this review, including five cases searched from the PubMed



Figure 1. Ultrasonography showed several mixed echoic nodules with calcification in the remnant right thyroid gland with maximal size about 3.1 cm×2.1 cm×2.0 cm (A), subcutaneous iso-echoic nodules with maximal size about 1.3 cm×1.0 cm×0.7 cm (B) in the right anterior neck and an iso-echoic nodule in the infraclavicular fossa in size of 2.4 cm×1.0 cm×0.9 cm (C).

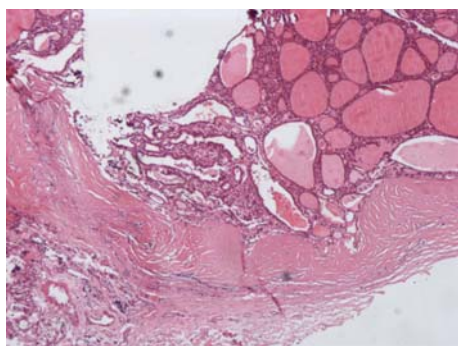


Figure 2. Histopathologic examination of all the nodules removed from the right thyroid and right neck confirmed the diagnosis of nodular goiter with adenomatous hyperplasia.

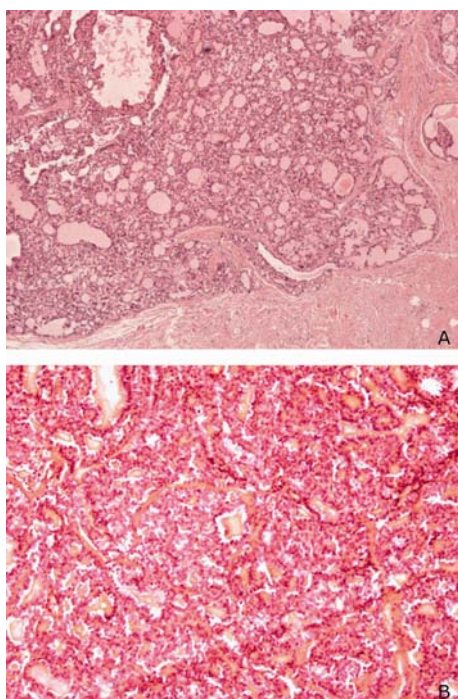


Figure 3. The subcutaneous nodule showed nodular goiter with adenomatous hyperplasia within fibrous connective tissue and skeletal muscle tissue. Immunostaining of galectin-3 was negative (A) and ki-67 labeling index of subcutaneous nodules was about 3% (B).

and one case from our hospital. Lee *et al*⁶ reported a 12-year-old female patient who suffered multiple subcutaneous implantations after endoscopic hemithyroidectomy with pathological diagnosis of adenomatous hyperplasia. Koh *et al*⁷ reported a 22-year-old female patient who suffered multiple implantations along the tracks of the trocars after endoscopic hemithyroidectomy with pathological diagnosis of adenomatous goiter. The rest three cases⁸⁻¹⁰ issued about patients who suffered implantations around the

previous operative tunnels or tracks of trocars after endoscopic thyroidectomy for thyroid cancer. Characteristics of six patients are shown in Table 1.

DISCUSSION

Prevalence

Extrathyroidal implantation of thyroid hyperplastic or neoplastic cells is a rare complication of endoscopic thyroid surgery. The prevalence of implantation after fine-needle aspiration biopsy in papillary thyroid carcinoma was 0.14% and mainly resulted in malignant thyroid tumors.⁵ However, no accurate statistical data can be found in open or endoscopic thyroid surgery.¹⁰ According to published research, only five cases reported on local recurrence or implantation after endoscopic thyroid surgery, of which two cases being benign thyroid diseases^{6, 11} and the other three being malignant.⁸⁻¹⁰

Pathogenesis and prevention

Multiple possible factors associated with the local recurrence of implantation can be analyzed as follow. Most essentially, surgical technique plays a decisive role.¹⁰ Previous studies demonstrated that with increase of surgical experience, risk of port-site metastases occurrence can be effectively and gradually reduced.¹² Secondly, instrument contamination during specimen manipulation may lead to implantation of subcutaneous tunnel, port-site or operative bed.¹³ Also, the chimney effect, which means that during the process of insufflation displacing tumor cells, the leaked gas along the trocars in thyroid endoscopic surgery^{11, 14, 15} causes the tumor cells to migrate around and be implanted at the canal wall, yielding to the gas flow. It should be noticed that the implanted cells are likely to become more invasive than those within thyroid on account of severe environment.¹⁶

In order to minimize the risk of implantation, a comprehensive preoperative evaluation should be completed. It requires meticulous intraoperative surgical treatment and scarification or rupture of tumor must be avoided. Avoiding cutting or rupture may lead to implantation. In addition, despite the divergent public opinion on this issue, the indications for endoscopic thyroidectomy should be strictly limited. The current existing indications include a benign single thyroid nodule less than 4 cm in diameter and a low-risk papillary carcinoma with nodules smaller than 1 cm.⁶ Miccoli *et al*¹⁷ reported that it can only be done under circumstances that the maximum diameter of nodules does not exceed 30 mm and the total volume of the thyroid glands not exceed 25 ml.

Table 1. Characteristics of six patients suffering from subcutaneous implantation of thyroid hyperplastic or neoplastic cells after endoscopic thyroid surgery

Authors	Age (yrs)	Sex	Size (cm)	Operation	Pathology	Interval between surgery and implantation	Number of implanted lesions	Location of implanted lesions
Our case	21	Female	2.2	Endoscopic right partial hemithyroidectomy	Multinodular goiter	5 years	Multiple	Subcutaneous fat layer and anterior cervical muscle
Lee <i>et al</i> ⁶	12	Female	5.5	Endoscopic hemithyroidectomy	Adenomatous hyperplasia	5 years	Multiple	Subcutaneous fat layer
Koh <i>et al</i> ⁷	22	Female	4.0	Endoscopic hemithyroidectomy	Adenomatous goiter	2 years	Multiple	Subcutaneous nodules located along the tracks of the trocars
Kim <i>et al</i> ⁸	25	Female	3.0	Endoscopic thyroidectomy	Thyroid cancer	14 month	Multiple	Recurrent cancers around the operative bed and subcutaneous tunnel
Hur <i>et al</i> ⁹	61	Female	4.4	Endoscopic thyroidectomy	Follicular thyroid cancer	31 months	Multiple	Around the operative bed and along the port insertion site
Li <i>et al</i> ¹⁰	39	Female	2.9	Endoscopic left hemithyroidectomy and open surgery with total thyroidectomy and bilateral central neck dissection	Papillary thyroid carcinoma	1 year	Multiple	Nodules around the scar and nodules located along the previous operative tunnels

Age: age at first procedure; size: maximal diameter of thyroid lesion at the time of the initial procedure.

Conditions for considering extrathyroidal implantation after the endoscopic thyroidectomy

When nodules were found outside the thyroid after endoscopic thyroidectomy, surgical implantation or metastatic lymph nodes must be put into consideration. Multiple subcutaneous nodules located in the previous subcutaneous endoscopic tunnel or operating field and resembling previous intrathyroid tumors on histology were consistent with intra-implantation or postoperative implantation.¹⁰

Therapies

The therapies include surgery, radioiodine therapy, and hormone suppression therapy. Among which surgery is the most effective treatment for both benign and malignant tumors. However, radioiodine therapy is required if the implants showed sufficient iodine uptake. Hormone suppressive therapy is generally used for prevention treatment if the implant growth is thyroid stimulating hormone-dependent.^{10, 11}

Prospect

As a whole, in spite of its advantages, inevitable defects along with endoscopic thyroidectomy cannot be ignored. It has a relatively long learning curve that requires larger

space of dissection, which leads to significant postoperative pain. Therefore, it cannot be yet recommended as a safe, feasible alternative to standard thyroidectomy. The continued heterogeneity in technique, lack of evidence-based studies, and continuous evolution of new techniques are further proof that the current axillary, chest wall, and breast access sites are not ready for mainstream operation. Recently, latest updated techniques have been proposed, including a dorsal approach, a trans-oral approach, a posterior auricular approach, and other robot-assisted approaches. However, the practical value of these techniques remains unclear at best for lack of evidence. Whether endoscopic thyroidectomy should replace open thyroidectomy as the standard for patient care with thyroid diseases is still highly controversial.

Conclusion

At present, most patients prefer endoscopic thyroid surgery rather than open ones owe to its excellent cosmetic results and rapid recovery. However, side effects such as headache implantation may occur in both benign and malignant disease. Therefore, a comprehensive preoperative evaluation and strict indications should be followed. Precautions against rupture of a nodule should be noticed whatever the nature of thyroid nodule is. Another

preventive measure during retrieval of surgical specimen is the use of specimen bag. The diagnosis should be suspected clinically when soft tissue nodules appear around the surgical field after endoscopic thyroid surgery. The incidence of implantation or recurrence is hopefully to be reduced via above mentioned measures.

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