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CASE REPORT

# Needle tract seeding of papillary thyroid carcinoma after fine-needle capillary biopsy: A case report

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**Author contributions:** Xie L conceived and designed the study; Shi LH, Zhou L, Xia L and Xie L contributed to the treatment of the case; Lei YJ performed the histological examination and confirmed the diagnosis; Xia L collected and analyzed data; Shi LH and Zhou L wrote the manuscript; Xie L revised the article and supervised the project; all authors read and approved the final manuscript.

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## Abstract

*BACKGROUND*

Fine-needle biopsy is an accurate and cost-efficient tool for the assessment of thyroid nodules. It includes two primary methods: Fine-needle capillary biopsy (FNCB) and fine-needle aspiration biopsy. Needle tract seeding (NTS) is a rare complication of thyroid fine-needle biopsy mainly caused by fine-needle aspiration biopsy rather than FNCB. Here, we present an extremely rare case of a papillary thyroid carcinoma (PTC) patient with FNCB-derived NTS.

*CASE SUMMARY*

We report a 32-year-old woman with PTC who showed subcutaneous NTS 1 year after FNCB and thyroidectomy. NTS was diagnosed based on clinical manifestations, biochemistry indices, and imaging (computed tomography and ultrasound). Pathological identification of PTC metastases consistent with the puncture path is the gold standard for diagnosis. Surgical resection was the main method used to treat the disease. After surgery, thyroid function tests and ultrasound scans were performed every 3-6 mo. To date, no evidence of tumor recurrence has been observed.

*CONCLUSION*

FNCB is a safe procedure as NTS is rare, and can be easily removed surgically with no recurrence. Accordingly, NTS should not limit the usefulness of FNCB.

**Key Words:** Needle tract seeding; Fine-needle capillary biopsy; Papillary thyroid

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carcinoma; Rearranged during transfection gene fusion; Thyroglobulin antibody; Case report



**Core Tip:** Needle tract seeding (NTS) of tumor cells is rare. Given that NTS is mainly caused by fine-needle aspiration biopsy rather than fine-needle capillary biopsy (FNCB), the FNCB-derived deposit of tumor cells has never been reported in papillary thyroid carcinoma. Here, we present a case of NTS caused by FNCB in a papillary thyroid carcinoma patient and performed whole-genome sequencing of the NTS-derived lesion. In this case, subtle changes in the patient's thyroglobulin and thyroglobulin antibodies were observed. Importantly, the information presented here will help improve the understanding of this disease.

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## INTRODUCTION

Fine-needle biopsy (FNB) is a reliable, accurate, and cost-effective technique to diagnose thyroid nodules, but it can lead to potential complications[1]. Of note, needle tract seeding (NTS) of tumor cells is a rare consequence[2,3]. Given that NTS is primarily caused by fine-needle aspiration biopsy rather than fine-needle capillary biopsy (FNCB), the FNCB-derived deposit of tumor cells has never been reported in papillary thyroid carcinoma (PTC)[4]. Here, we present a case of NTS caused by FNCB in a PTC patient and the follow-up of clinical characteristics after the removal of seeding lesions. A genetic investigation was performed by whole-genome sequencing (WGS) of the NTS-derived lesion. In this study, we determined that FNCB should be carefully performed to minimize the potential of NTS in the clinical setting[2].

## CASE PRESENTATION

### *Chief complaints*

A 32-year-old woman was admitted to our hospital due to the presence of anterior neck nodules for 3 years.

### *History of present illness*

The patient presented with a 3-year history of a 3-mm subcutaneous nodule in the right side of her neck that was initially diagnosed as a sebaceous cyst. As the nodule was stable in terms of size, morphology, and color, the patient was followed-up without treatment. As the patient was willing to have the nodule removed, she was admitted to our hospital.

### *History of past illness*

The patient underwent ultrasound-guided FNCB (22-gauge needles) of bilateral thyroid nodules and lateral cervical lymph nodes performed by Zhou L in 2014 (ultrasound performance is shown in Figure 1A-D). The pathologist reported that the nodules and lymph nodes were tumorous. Subsequently, total thyroidectomy followed by bilateral modified neck dissection, including bilateral levels II, III, IV, and VI, were performed. Histologically, the largest of the three PTC nodules was 2 cm × 1.6 cm and showed extra-thyroidal extension (Figure 1E), and 29 of 134 lymph nodes were malignant. Subsequently, 100-mCi radioactive iodine therapy was administered. Imaging examinations, including ultrasound and functional scans, showed no sign of a tumor.

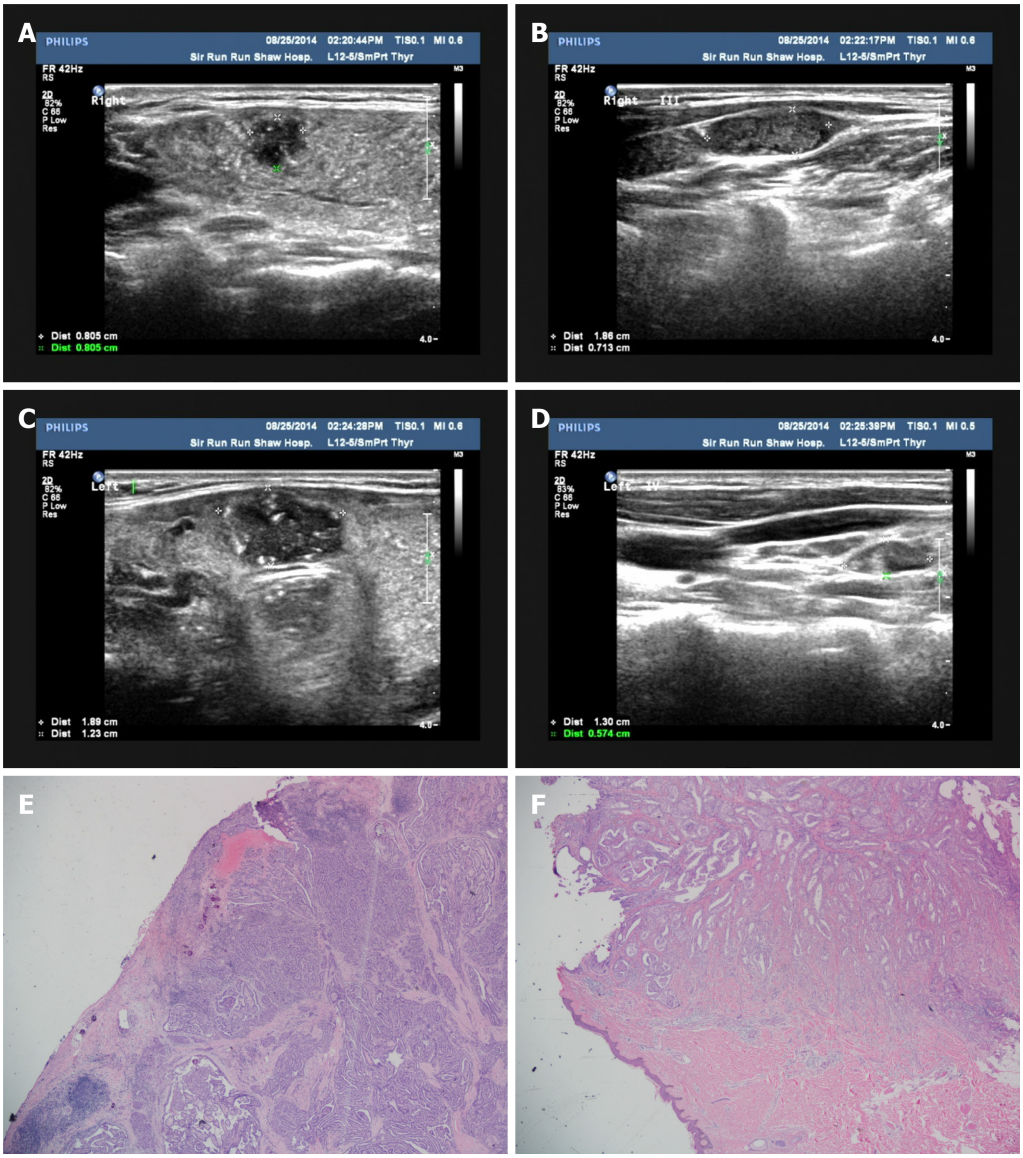



**Figure 1 Ultrasonography and histopathology.** A: Ultrasound image of the largest primary papillary carcinoma in the right thyroid lobe; B: Ultrasound image of a suspicious malignant lymph node in the right lateral neck of level III; C: Ultrasound image of the largest primary papillary carcinoma in the left thyroid isthmus; D: Ultrasound image of a suspicious malignant lymph node in the right lateral neck of level IV. E: Hematoxylin-eosin staining of the largest thyroid nodule, 40 × magnification; F: Hematoxylin-eosin staining of the subcutaneously implanted nodule, 40 × magnification.

### *Personal and family history*

No specific personal or family history of the disease was recorded.

### *Physical examination*

An old, well-healed traverse surgical scar on the middle of the neck was observed. A hard 3-mm subcutaneous mass with poor mobility was palpable on the right side of the neck, and there were no other positive signs on physical examination.

### *Laboratory examinations*

After thyroid surgery, thyroid-stimulating hormone (TSH) levels were maintained between 0.01 mIU/L and 0.04 mIU/L with TSH suppressive therapy, and thyroglobulin (Tg) was stable below 0.03 ng/mL. However, the Tg antibody (Tg-Ab) level tended to fluctuate during various stages of the disease. Initially, Tg-Ab decreased persistently but then began to increase when the patient was pregnant for 2 mo.

### *Imaging examinations*

All routine imaging examinations were unremarkable.

## FINAL DIAGNOSIS

The diagnosis before surgical resection was a sebaceous cyst.

## TREATMENT

The subcutaneous nodule was removed. During surgery, a deposit was observed in the skin and sternocleidomastoid muscle, consistent with the location of the puncture needle path of the right lateral cervical lymph nodes. The linear array and site of the nodule indicated that seeding most likely resulted from the needle biopsy.

## OUTCOME AND FOLLOW-UP

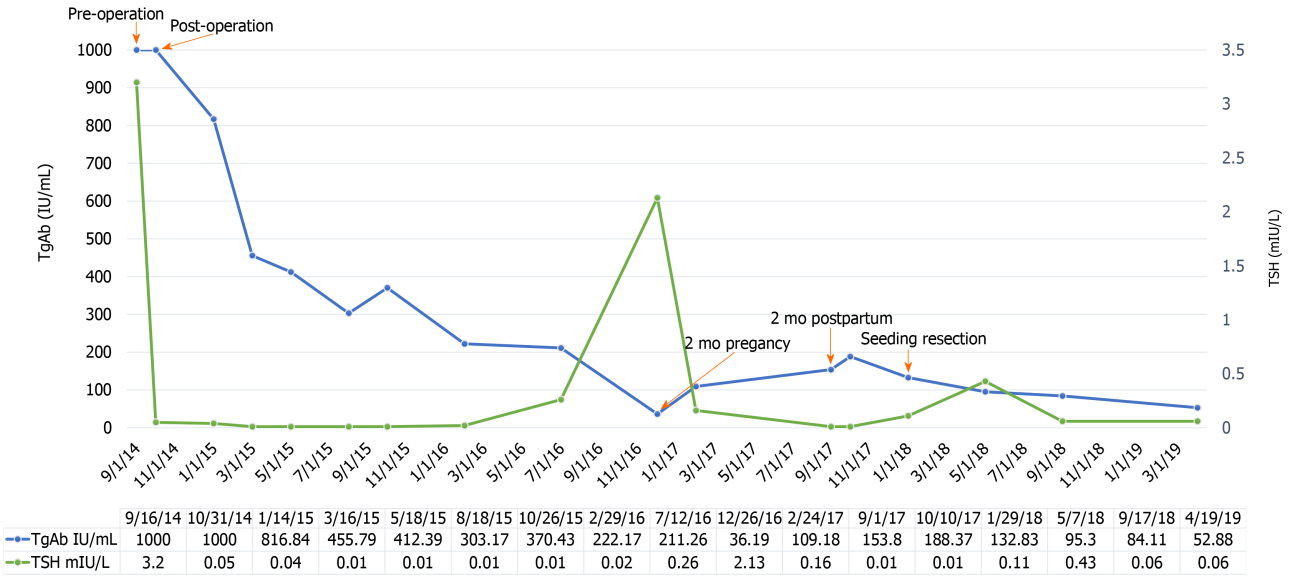
Microscopic examination revealed a non-enveloped tumor with a large number of luminal structures in the dermis. The walls of the tubes were composed of a single layer of columnar cells with lightly stained nuclei and eosinophilic lumen, and infiltration of cells with strong nuclear staining was detected (Figure 1F). Based on the immunohistochemical results showing positive staining for thyroid transcription factor and Tg, the lesions were pathologically diagnosed as PTC metastases. In addition, WGS was performed to analyze the NTS-derived lesion, and coiled-coil domain containing 6 (*CCDC6*)-rearranged during transfection (*RET*) fusion was detected. When the subcutaneous nodule was removed, the Tg-Ab level declined rapidly and showed a downward trend in the following days (Figure 2). To date, no evidence of tumor recurrence has been observed.

## DISCUSSION

FNB has been used to evaluate thyroid nodules for over 50 years[5]. Worldwide, thousands of FNBs for thyroid nodules are performed annually, with few reported cases of NTS[2,6] (approximately 20 cases)[7-12]. Previously, Ito *et al*[9] uncovered a higher incidence of NTS in PTC patients (0.14%) than expected, as several NTS cases were asymptomatic[12]. The most typical clinical sign of NTS was the presence of linearly arranged masses between the penetrated point and primary tumor[8,10]. However, some cases only exhibited small subcutaneous nodules at the penetrated point[7,12]. In the present case, the surgeon did not separate the skin and subcutaneous tissue layer during surgery, and most of the implants were located in the subcutaneous tissue layer. Therefore, we believe that the subcutaneous nodule caused by FNCB was possibly greater than that in the initial surgery. Generally, the clinical features (*e.g.*, Tg, Tg-Ab, and others) of NTS in PTC patients are not fully understood. In this case, the Tg-Ab level increased with the development of the subcutaneous lesion but decreased immediately after surgical resection. This suggests that the Tg-Ab level may be an earlier biomarker in some NTS patients, but further investigations are warranted.

Several needle-associated risks of NTS, such as damage caused by the needle size, number of passes, withdrawing the needle without releasing suction, and injecting the tumor at the time of biopsy, have been well-documented[2,4,9]. Technically, FNB can be performed with aspiration using a syringe (fine-needle aspiration biopsy) or without aspiration (FNCB). Theoretically, NTS is rarely caused by FNCB as FNCB minimizes tissue and cell trauma[13]. However, our case indicates that FNCB is not as safe as we expected. Given that tumor cells are easily spread by aspiration, especially using a needle with a large diameter, non-aspiration techniques (*i.e.*, FNCB) with a 23-G or a smaller fine needle are recommended[14,15]. In any case, an excessive number of passes should be avoided[16].

Mechanistic investigation of thyroid cancer cell implantation and growth provides a better understanding of the pathogenesis underlying NTS. Several genetic mutations have been identified in thyroid cancers, such as in *RAS, BRAF, P53,* and *TSHR* genes[17,18]. Khan *et al*[18] reported that *RET/PTC3* rearrangements were significantly associated with gender, lymph node metastasis, and elevated TSH levels. Similarly, our female patient presented with Hashimoto thyroiditis, an elevated TSH level, and lymph node metastasis. In addition, *RET* mutations and rearrangements closely associated with tumor proliferation, invasion, and migration may be risk factors for




| | 9/16/14 | 10/31/14 | 1/14/15 | 3/16/15 | 5/18/15 | 8/18/15 | 10/26/15 | 2/29/16 | 7/12/16 | 12/26/16 | 2/24/17 | 9/1/17 | 10/10/17 | 1/29/18 | 5/7/18 | 9/17/18 | 4/19/19 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| TgAb IU/mL | 1000 | 1000 | 816.84 | 455.79 | 412.39 | 303.17 | 370.43 | 222.17 | 211.26 | 36.19 | 109.18 | 153.8 | 188.37 | 132.83 | 95.3 | 84.11 | 52.88 |
| TSH mIU/L | 3.2 | 0.05 | 0.04 | 0.01 | 0.01 | 0.01 | 0.01 | 0.02 | 0.26 | 2.13 | 0.16 | 0.01 | 0.01 | 0.11 | 0.43 | 0.06 | 0.06 |

**Figure 2 The fluctuations in thyroglobulin antibody and thyroid-stimulating hormone levels.** TgAb: Thyroglobulin antibody; TSH: Thyroid-stimulating hormone.

NTS. *RET* fusions or rearrangements are somatic juxtapositions of 5' sequences from other genes with 3' *RET* sequences encoding a tyrosine kinase[19]. *RET* rearrangements (at least 13 different *RET* fusions) occur in approximately 2.5%-73.0% of sporadic PTC patients[20,21]. The most prevalent *RET* fusions are *CCDC6-RET* (also known as *RET/PTC1*) and nuclear receptor co-activator 4 *(NCOA4)-RET* (also known as *RET/PTC3*)[22-25]. In our case, the fusion type was *ERC1-RET*, which has not been previously reported.

For medical exploration and rigorous evaluation, WGS was performed to analyze the NTS-derived lesion in the patient free of charge. After the NTS-derived lesion was removed, no evidence of tumor recurrence was observed. Therefore, the patient is satisfied with the treatment and results and is currently being followed-up in our hospital.

## CONCLUSION

FNB is a sensitive and specific technique for diagnosing thyroid nodules preoperatively, thereby facilitating the determination of optimal treatment plans for PTC[26,27]. Although NTS is a potential complication of FNB, surgical resection of NTS-derived lesions offers a favorable prognosis. Serum biomarkers and genetic characteristics could help in the treatment and follow-up of PTC patients with NTS.

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