Clinical significance and cytological detection of tracheal puncture following thyroid fine-needle aspiration: A retrospective study

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Abstract
Background: There have been no detailed reports on tracheal puncture after thyroid fine-needle aspiration (FNA). This study aimed to discuss the cytological differential diagnoses of tracheal puncture after thyroid FNA and clarify its clinical significance.

Methods: Tracheal puncture was defined as aspiration of tracheal components, including ciliated cells, chondrocytes, and goblet cells. A history of air suction or cough during aspiration was also considered tracheal puncture. Among the 18,480 nodules from 13,813 patients that underwent thyroid FNA, 70 (0.38%) nodules with tracheal puncture were retrospectively examined. Eleven thyroglossal duct cysts (TGDCs) and seven bronchial cysts that could exhibit ciliated cells were included in the study to compare the cytological findings.

Results: Sixty-six (94.3%) nodules had no clinical evidence of complications during and after FNA. Of the nodules with tracheal puncture, 64.3%, 48.6%, and 51.4% nodules were <1.0 cm in size, located in the isthmus, and associated with calcification. Cytological examination showed that chondrocytes and ciliated cells were present in 94.3% and 32.9% nodules, respectively. Ciliated cells seen in nodules with tracheal puncture and TGDCs were non-degenerative, whereas those in bronchial cysts were degenerative.

Conclusion: Tracheal puncture after thyroid FNA is rarely noticed clinically, does not cause serious conditions, and spontaneously resolves. This complication more likely occurs in small-calcified nodules in the isthmus. Chondrocytes are more reliable diagnostic clues than ciliated cells to indicate tracheal puncture cytologically.

Keywords
chondrocyte, ciliated cell, complication, fine-needle aspiration, thyroid, tracheal puncture
1  |  INTRODUCTION

Fine-needle aspiration (FNA) cytology is a simple, reliable, and generally safe diagnostic tool that has been widely used in the management of thyroid nodules. Local pain, discomfort, and minor hemorrhage are common complications of thyroid FNA.\(^1\)\(^-\)\(^3\) but serious complications are extremely rare.\(^4\)\(^-\)\(^7\) Moreover, tracheal puncture after thyroid FNA may also clinically manifest as cough, hemoptysis, or air suction during aspiration.\(^4\)\(^,\)\(^8\)\(^,\)\(^9\) Cytologically, the presence of ciliated cells indicates accidental penetration of the needle into the trachea.\(^4\)\(^,\)\(^10\)\(^-\)\(^13\) To the best of our knowledge, there have been no detailed reports on tracheal puncture after thyroid FNA. Therefore, this study aimed to discuss the cytological differential diagnoses of tracheal puncture after thyroid FNA and clarify its clinical significance. We also discussed the differential diagnosis of bronchial and thyroglossal duct cysts (TGDCs) containing ciliated cells that can be confused with thyroid lesions on ultrasound examinations.

2  |  MATERIALS AND METHODS

Ethical approval was obtained from the ethics committee of our hospital. The study protocol was reviewed and approved by the Institutional Review Board of Kuma Hospital (210610–1). We reviewed the cytology report database of 13,813 patients with 18,480 thyroid nodules who underwent FNA at Kuma Hospital from January 2018 to December 2019. Clinical and cytological data were obtained from the medical records of patients at Kuma Hospital. All findings and test results in the electronic medical records (HOPE Cloud Chart, Fujitsu, Tokyo, Japan) and pathology reporting system (CNA-Net, Sakura Finetek Japan Co, Tokyo, Japan) were stored in the data warehouse. We extracted relevant data by keyword search from the database.

Ultrasound-guided FNA was performed using a 22-gauge needle without local anesthesia. The needle was inserted in a plane perpendicular to the scanning plane (perpendicular positioning).\(^14\) Smears were prepared using the press and release method and subsequently stained with Papanicolaou stain. When bloody samples were aspirated, we removed the blood components by tilting the glass slides immediately after the samples were expressed on the slides.

Tracheal puncture was defined as aspiration of tracheal components, including ciliated cells, chondrocytes, and goblet cells. A history of air suction or cough during aspiration was also considered tracheal puncture. Of the 18,480 nodules, 70 (0.38%) nodules with tracheal puncture were retrospectively examined. Calcification patterns were classified based on the method proposed by Kobayashi et al.\(^15\) In addition, to discuss the cytological differential diagnoses, two lesions that were located near the thyroid and could exhibit ciliated cells were included in the present study; 11 TGDCs and seven bronchial cysts were identified.

3  |  RESULTS

3.1  |  Clinical findings

Of the 70 nodules with tracheal puncture, 66 (94.3%) nodules had no clinical evidence of complications during and after FNA. In three (4.3%) nodules, air was aspirated into the syringe during puncture. In the remaining one case, the patient coughed immediately after puncture. However, patients did not receive any intervention for their episodes. There were no cases with aspiration of mucous material or bloody sputum.

3.2  |  Ultrasound findings

The size and number of nodules with tracheal puncture were as follows: <5 mm, 15 (21.4%); 6–10 mm, 30 (42.9%); 11–15 mm, 16 (22.9%); and >16 mm, 9 (12.9%). Further, 34 (48.6%), 19 (27.1%), and 16 (22.9%) nodules were located in the front of the trachea, right lobe, and left lobe, respectively; the location of the remaining one (1.4%) nodule was unknown. Calcification was observed in 36 (51.4%) nodules. Massive and fragmentary (measuring >3 mm) calcifications were observed in 19 (52.8%) and 10 (27.8%) nodules, respectively. Punctate (<1 mm) and/or speckled (1–3 mm) calcifications were observed in seven (19.4%) nodules. Egg shell-type calcifications were not observed.

3.3  |  Original cytology reports

Table 1 shows the original cytology reports of thyroid nodules with tracheal puncture after FNA. There were 26 (37.1%), 21 (30.0%), and 16 (22.9%) benign, nondiagnostic or unsatisfactory (ND/UNS), and malignant nodules, respectively. Furthermore, all 16 malignant nodules were classified as papillary carcinoma.

3.4  |  Cytological findings

Table 2 summarizes the cytological findings of tracheal puncture, TGDCs, and bronchial cysts. Of the 70 nodules with tracheal puncture, 66 (94.3%) nodules exhibited chondrocytes. Chondrocytes were round to oval in shape and showed small nuclei with abundant lacunae surrounded by violet stroma (Figure 1A). They appeared either individually or in clusters. Tissue fragments measuring 28.6–500 μm and comprising several chondrocytes and cartilage matrix were also observed (Figure 1B). The cartilage matrix varied in color (milky white, violet, or light green). Among the 66 nodules exhibiting chondrocytes, 43 (61.4%) nodules exhibited no other findings suggestive of tracheal puncture.

Ciliated cells and goblet cells were found in 23 (32.9%) and eight (11.4%) nodules, respectively. Ciliated cells appeared as either single cells or cell clusters with palisading. Moreover, ciliated cells were well...
preserved with prominent cilia and terminal plates (Figure 2A). All the four nodules that were clinically identified as having tracheal puncture exhibited both chondrocytes and ciliated cells. Goblet cells appeared mixed with clusters of ciliated cells. Three (4.3%) nodules showed lightly pink-stained mucous material in the background (Figure 1C). In addition, small squamous cells with keratinization were observed in three (4.3%) nodules (Figure 3). Dust cells were not observed.

In three (27.3%) cases of TGDCs, well-preserved ciliated cells were observed (Figure 2B). Two TGDCs showed squamous epithelium. Chondrocytes were not observed in any of the cases. Foamy histiocytes, proteinaceous material, and necrotic materials were observed in all, six (54.5%), and three (27.3%) cases, respectively. The necrotic materials observed in TGDCs seemed to be derived from foamy histiocytes. Lastly, bronchial cysts showed degenerative or

**Table 1** Original cytology reports of thyroid nodules with tracheal puncture after fine-needle aspiration

| Categories                                                                 | Suggestive diagnosis                       |
|---------------------------------------------------------------------------|--------------------------------------------|
| I. Nondiagnostic or unsatisfactory                                       | 21 (30.0%)                                 |
| II. Benign                                                                | 26 (37.1%)                                 |
| Benign lesion                                                             | 17                                          |
| Chronic thyroiditis                                                       | 4                                           |
| Adenomatous nodule                                                       | 5                                           |
| III. Atypia of undetermined significance or follicular lesion of undetermined significance | 6 (8.6%)                                    |
| Cannot be ruled out papillary carcinoma                                   | 4                                           |
| Adenomatous nodule or follicular tumor                                    | 1                                           |
| Papillary carcinoma or follicular tumor                                   | 1                                           |
| IV. Follicular neoplasm or suspicious for a follicular neoplasm           | 1 (1.4%)                                    |
| Follicular tumor                                                          | 1                                           |
| V. Suspicious for malignancy                                              | 0 (0%)                                      |
| VI. Malignant                                                             | 16 (22.9%)                                  |

**Table 2** Cytological findings of tracheal puncture, thyroglossal duct cysts, and bronchial cysts

|                          | Tracheal puncture (70 nodules) | Thyroglossal duct cyst (11 lesions) | Bronchial cyst (7 lesions) |
|--------------------------|--------------------------------|-------------------------------------|---------------------------|
| Mucous material          | 3 (4.3%)                       | 0 (0%)                              | 0 (0%)                    |
| Proteinaceous material   | 2 (2.9%)                       | 6 (54.5%)                           | 1 (14.3%)                 |
| Necrotic materials       | 0 (0%)                         | 3 (27.3%)                           | 4 (57.1%)                 |
| Foamy histiocytes        | 9 (12.9%)                      | 11 (100%)                           | 4 (57.1%)                 |
| Chondrocytes             | 66 (94.3%)                     | 0 (0%)                              | 0 (0%)                    |
| Ciliated cells           | 23 (32.9%) (non-degenerative)   | 3 (27.3%) (non-degenerative)         | 7 (100%) (5: degenerative) |
| Goblet cells             | 8 (11.4%)                      | 0 (0%)                              | 1 (14.3%)                 |
| Squamous cells           | 3 (4.3%)                       | 2 (18.2%)                           | 0 (0%)                    |

**Figure 1** Tracheal puncture. (A) Chondrocytes with abundant lacuna are seen (Papanicolaou stain, ×400). (B) Tissue fragment comprising chondrocytes and cartilage matrix are seen (Papanicolaou stain, ×200). (C) Lightly pink-stained mucous material is seen in the background; note some chondrocytes (arrow) (Papanicolaou stain, ×400) [Color figure can be viewed at wileyonlinelibrary.com]
necrotic ciliated cells (n = 5, 71.4%) (Figure 2C), whereas chondrocytes and mucous material were not observed.

3.5 | Pathological findings

Of the 70 nodules with tracheal puncture, 13 (18.6%) nodules were resected and microscopically examined. All nodules were classified as papillary carcinomas. Moreover, 10 (76.9%) nodules with papillary carcinoma were associated with calcification, ossification, and/or hyalinization. No findings related to tracheal puncture were observed.

4 | DISCUSSION

Tracheal puncture is an unavoidable complication of FNA because of the anatomical location of the trachea.\textsuperscript{4,8,9} However, there have been no detailed studies on this complication. Clinically, tracheal puncture can be detected by aspiration of air into the syringe, hemoptysis, or cough during or immediately after puncture.\textsuperscript{4,8,9} However, cytologically, tracheal puncture can be identified based on the presence of chondrocytes or ciliated cells.\textsuperscript{4,10–13} Silverman et al. reported one (0.3%) case of tracheal puncture among 309 thyroid FNA cases.\textsuperscript{8} However, the identification of tracheal puncture was not described. Kumar and Omrani reported that three (0.9%) of 339 thyroid aspirates exhibited ciliated columnar cells due to accidental penetration of the needle into the trachea.\textsuperscript{10} Jayaram observed respiratory epithelial cells in 42 (0.2%) of 18,847 thyroid FNA cases.\textsuperscript{11} In the current study, the incidence of tracheal puncture after observing cytological specimens was 0.38%, of which 4.3% cases were clinically identified; no intervention was performed for this complication. Most tracheal punctures were clinically overlooked, did not cause serious disability, and resolved spontaneously.

The frequency of tracheal puncture largely depends on the location, size, experience of the aspirators, and needle insertion procedure. Small lesions in the isthmus are risk factors for this complication.\textsuperscript{10,13} In our study, approximately two-thirds and half of the nodules with tracheal punctures were small (size: <1 cm) lesions and located in the isthmus, respectively. There were two needle insertion approaches—perpendicular and parallel. The former approach...
was associated with a higher risk of tracheal puncture than the latter approach because the trachea was located just below the lesions of the isthmus on ultrasound. To reduce the risk, we recommend moving the nodule laterally using a probe before puncturing (Figure 4). We use 22-gauge needles for thyroid cytology in our daily practice, as do other institutions in Japan. If smaller needles were used, as in Europe and the United States, tracheal punctures would be safer and less common.

In cases with tracheal puncture, incidences of ND/UNS and malignant nodules were higher than those of each category described so far. The former might be due to the difficulty in taking a route that avoids the trachea, and the small size of the nodule. In the latter cases, microcarcinomas located near the trachea are considered for resection, so it is necessary to diagnose them by cytology despite their small size. Calcifications were observed in approximately half of the cases. Since the general frequency of calcification in thyroid nodules is 27%, the frequency of calcification in thyroid nodules with tracheal punctures is clearly higher. There were two possible reasons for the association between calcifications and tracheal puncture. One reason for this was the difficulty in observing the needle tip within the calcified nodule using ultrasound. The other reason was the deeper penetration of the needle tip in the calcified nodule due to excessive force.

Cytologically, tracheal puncture was assumed to be due to the presence of tracheal components, including chondrocytes, ciliated cells, goblet cells, keratinized squamous cells, and mucous material. In the present study, chondrocytes were most frequently observed (94.3%), followed by ciliated cells (32.9%), and goblet cells (11.4%). When the lesions of the isthmus were punctured using the perpendicular approach, chondrocytes are more likely to be aspirated than ciliated cells (Figure 5). In cases where chondrocytes are present in the absence of ciliated cells, the needle tip does not penetrate the trachea and is presumably less clinically symptomatic. In such cases, there would be no need to exaggerate this as a complication of tracheal puncture. Cases using the parallel method will likely yield different results. Chondrocytes are not normally present in the thyroid gland. Therefore, their presence was a reliable indicator of tracheal puncture.

In contrast, ciliated cells can also be seen in TGDCs and bronchial cyst, and can be confused with thyroid lesions on ultrasound examinations. TGDCs can occur along the path of the thyroglossal duct, from the base of the tongue to the suprasternal notch. When cystic lesions arising in the isthmus exhibited ciliated cells and not chondrocytes, it was difficult to distinguish tracheal puncture from a TGDC. TGDCs occurring near the thyroid should be recognized as a pitfall for tracheal puncture. We demonstrated that ciliated cells observed in bronchogenic cysts were degenerative, whereas those observed in nodules with tracheal puncture were not degenerative. These findings may provide diagnostic clues to distinguish between nodules with tracheal puncture and bronchogenic cysts.

In conclusion, tracheal puncture after thyroid FNA is rarely noticed clinically, does not cause serious conditions, and spontaneously resolves. This complication more likely occurs in small-calcified nodules in the isthmus. Chondrocytes are more reliable diagnostic clues than ciliated cells to indicate tracheal puncture cytologically.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

AUTHOR CONTRIBUTION
All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Aki Tanaka, Miyoko Higuchi, Risa Kanematsu, and Naoki Yamao. The first draft of the manuscript was written by Aki Tanaka and Mitsuyoshi Hirokawa. Ayana Suzuki, Toshitetsu Hayashi, Seiji Kuma, and Akira Miyauchi commented on previous versions of the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author, A.T., upon reasonable request.

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FIGURE 5  When puncturing the lesions of the isthmus using the perpendicular approach, chondrocytes are more likely to be aspirated than ciliated cells [Color figure can be viewed at wileyonlinelibrary.com]
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