

Rare potential complications of thyroid fine needle biopsy

Polyzos SA¹, Anastasilakis AD²

¹2nd Internal Medicine Department, Medical School, Aristotle University of Thessaloniki, Hippokratia Hospital, Thessaloniki, Greece

²Department of Endocrinology, 424 Military Hospital, Thessaloniki, Greece

Abstract

Thyroid fine needle biopsy (FNB) is the procedure of choice for the management of thyroid nodules. Serious complications after FNB are rare, but there is also an underestimation of complication risk because of record, selection and publication biases. Hypothesis: Apart from the well-documented post-FNB complications, we hypothesized that there are potential complications following FNB, albeit supported by limited evidence in the literature. According to our hypothesis, there may be five distinct expected rare complications: 1) cyst fluid leakage; 2) anaphylactic reaction; 3) pneumothorax; 4) thromboembolism and 5) needle tract seeding of medullary thyroid carcinoma (MTC) or thyroid lymphoma.

Conclusions: Cyst fluid leakage and pneumothorax may be of minimal clinical significance. Needle tract seeding of MTC or thyroid lymphoma may not have significant clinical consequences, if someone considers the easiness and effectiveness of surgical removal of needle tract seeding in cases of differentiated thyroid carcinoma. On the contrary, anaphylactic reaction or thromboembolism may be life-threatening. The performers of thyroid FNB are hereby encouraged to publish these complications, if they ever occur, because awareness of them could render FNB even safer. Hippokratia 2011; 15 (2): 116-119

Key words: anaphylactic reaction; fluid leakage; fine-needle biopsy; needle tract seeding; pneumothorax; thyroid nodule; tromboembolism, review

Corresponding Author: Stergios Polyzos, 13 Simou Lianidi Str., 55134, Thessaloniki, Greece, Tel.: +30 2310 424710, Fax: +30 2310 424710, E-mail: stergios@endo.gr

Thyroid nodules are common in clinical practice and they are usually benign. Their risk of malignancy is low, but not negligible and it is necessary to be excluded¹. Thyroid fine needle biopsy (FNB) is the procedure of choice in the management of thyroid nodules, because of its simplicity, accuracy and cost-effectiveness¹⁻⁴. According to FNB result, the physician makes a decision whether the patient should be subjected to surgery or to follow-up. Recent surveys have emphasized that almost all endocrinologists use FNB in the diagnostic approach of thyroid nodules². The introduction of FNB in clinical practice has displaced the use radionuclide thyroid scan, at least in cases of normal or high thyroid stimulating hormone (TSH)⁵, and has almost halved the percentage of patients undergoing thyroidectomy⁶, thereby declining unnecessary imaging, operative morbidity and mortality and the cost of medical care. Technically, FNB can be performed with aspiration using a syringe [fine needle aspiration, (FNA)] or without aspiration [fine-needle capillary (FNC)] and can be guided only by palpation [palpation-guided FNB (P-FNB)] or by ultrasound [ultrasound-guided FNB (US-FNB)]⁷.

Clinical, histological and biochemical complications following thyroid FNB were recently reviewed. Post-FNB local pain and minor hematomas are the most common clinical complications^{8,9}. Post-FNB hemorrhage and fibrosis are the most common histological alterations

observed in surgical specimens, if thyroidectomy follows; however, some worrisome histological alterations mimicking thyroid malignancy may also be observed in benign nodules¹⁰. FNB can also trigger biochemical alterations in serum, since it may destroy thyroid follicles, resulting in thyroglobulin release into the circulation¹¹. Serious complications after FNB are rare, but there is also an underestimation of complication risk because of record, selection and publication bias. Furthermore, complications may be underreported because of the unwillingness of the performer to publish them⁸. The aim of this hypothesis is to encourage the performers of thyroid FNB to publish these complications, when they occur.

Hypothesis

Based on our previous experience^{8,10,11}, we hypothesized that there are potential complications following diagnostic thyroid FNB, which have not been reported in the literature yet or existing data are insufficient to support them. In order to confirm the lack of related evidence, we repeated a computerized advanced search for primary evidence in the PubMed and EMBASE electronic databases, as elsewhere reported^{8,10,11}, but data retrieval were minimal and inconclusive. According to our hypothesis, there may be five distinct expected but still unpublished complications: 1) cyst fluid leakage; 2) anaphylactic reaction; 3) pneumothorax; 4) thromboembolism and 5)

needle tract seeding of medullary thyroid carcinoma or thyroid lymphoma. These potential complications have been reported after similar techniques applied on the thyroid or after fine-needle biopsy on other organs.

Cyst fluid leakage

Fluid leakage from a cystic thyroid nodule into "normal" thyroid tissue surrounding the nodule (perinodular) or other tissues in vicinity to thyroid (perithyroidal) is a potential post-FNB complication. In a comprehensive review from the National Cancer Institute (NCI) Thyroid fine-needle aspiration State of the Science Conference regarding techniques for thyroid FNA, cyst fluid leakage is reported as an acute complication that may cause tenderness. It is thereby suggested that the performer should use a less aggressive technique and avoid excessive number of passes on cystic nodules in order to minimize this risk¹². However, to our knowledge, no case or case series have been reported to date, although fluid leakage is a rational consequence of FNB performed on cystic thyroid nodules. Fluid leakage after diagnostic FNB has been reported in other tissues, including cystic craniopharyngiomas¹³ and pancreatic cysts¹⁴. In the case of pancreatic cysts, fluid leakage may trigger pancreatitis¹⁴. Thyroid cyst fluid does not contain enzymes capable of triggering a similar condition, i.e., acute thyroiditis, but the triggering of mild thyroiditis and/or subsequent fibrosis of thyroid tissue cannot be excluded.

Ethanol leakage has been described after percutaneous ethanol injection (usually through a fine-needle under ultrasound guidance), which is a therapeutic method for cystic thyroid nodules¹⁵. Ethanol leakage may cause local pain and fibrosis in the surrounding tissues. We could hypothesize that it is actually a mixture of ethanol and cyst fluid leakage rather than pure ethanol leakage, which is caused by the increase of intranodular pressure after ethanol injection. Progressive disappearance of the perithyroidal abnormality on the ultrasound (U/S) and no significant alterations on thyroid function tests were reported during the follow-up of such cases¹⁵. Although controversy exists, some authors suggest complete evacuation of infused ethanol in order to prevent ethanol leakage¹⁵.

Anaphylactic reaction

Anaphylactic reaction is another potential complication of thyroid FNB. The use of local anesthetics, mainly lidocaine, or the rupture of a parasitic cyst, mistaken for a simple cystic thyroid nodule, might act as stimuli for anaphylactic reactions.

To our knowledge, there is no evidence of anaphylactic reaction to local anaesthetics used before thyroid FNB. There are mainly two reasons, apart from the unwillingness of the performer to publish them: 1) the use of lidocaine or similar local anesthetics are generally safe in low dose and hypersensitivity to them is uncommon; 2) local anaesthetics are used before FNB only in selected patients, i.e. painphobic patients, patients with deep-seated nodules or children younger than 7 years⁸. However,

there are some cases of local or even life-threatening systemic anaphylactic reactions after local anesthesia given for other reasons, mainly for dental procedures¹⁶⁻¹⁸. All physicians should consider systemic anaphylactic reaction in patients with rapid vascular collapse and respiratory failure immediately after local anaesthetics administration for minor outpatient procedures¹⁶. Complete medical history may partially prevent anaphylactic reaction, while co-administration of epinephrine may minimize the risk¹². If anaphylactic reaction occurs, emergent reaction is required, including administration of epinephrine and other resuscitative measures.

A case of transient anaphylactic reaction after FNB of a palpable nodule of the pretibial region has been reported. Histological examination of the nodule showed granulomatous reaction to cysticercosis¹⁹. Cysticercosis of the thyroid gland has been reported^{20,21}, but it usually represents the thyroid participation in generalized cysticercosis found in immunocompromised patients. Therefore, the diagnosis of cysticercosis is established before the thyroid lesions are mistaken for simple thyroid cystic nodules and are subjected to FNB. However, other parasitic cysts might more easily be mistaken for simple thyroid cystic nodules, because their primary lesion may be in the thyroid. Primary hydatid cysts of the thyroid due to echinococcosis, although rare, have been reported²²⁻²⁶ to be solitary or multiple cystic nodules of varying size. They can become very large (8-10 cm in diameter), because of the compressibility of the thyroid gland and adjacent tissues, and may cause obstructive symptoms, such as dyspnea²⁶. If echinococcosis has not initially been considered in the differential diagnosis, hydatid cyst might be subjected to FNB; such a mistake has been reported in other organs²⁷. However, FNB in a hydatid cyst could result in anaphylaxis and even in sudden death²⁸. If it does not occur, dissemination of daughter hydatid cyst is also a potential complication²⁹. U/S imaging is helpful in the diagnosis of echinococcosis, demonstrating the hydatid sand in purely cystic lesions as well as floating membranes, daughter cysts and vesicles. If a thyroid cystic nodule has ultrasonographic characteristics of a hydatid cyst, FNB should be avoided and the patient should be subjected to thyroidectomy. Serologic tests may also be used preoperatively, but they all have low diagnostic sensitivity and specificity and should be used in the follow-up of patients after treatment rather than the initial diagnosis²⁹. The rarity of thyroid echinococcosis and the unawareness of the physician may lead to FNB of a hydatid cyst with undesirable consequences. Medical history, including family history, patient's occupation and patient's residence, may be indicative of a thyroid hydatid cyst and is hereby highly suggested.

Pneumothorax

Pneumothorax is common after transcutaneous lung FNB and may occasionally occur after FNB in the breast and in axillary lymph nodes³⁰⁻³². In these cases, pneumothorax usually resolves spontaneously and its risk is

minimized, if 25-G or smaller needles are used³³. Thyroid FNB in supraclavicular or deep-seated thyroid nodules or in substernal multinodular goiter could theoretically result in pneumothorax due to apical pleural injury. We found no published case in our systematic search. Although there is no evidence, we believe that in case of pneumothorax after thyroid FNB the morbidity would be minimal, since it is usually a self-limited condition. However, it is highly suggested that supraclavicular or deep-seated thyroid nodules should be biopsied under U/S guidance. Furthermore, symptoms such as intense pain and dyspnea after FNB in supraclavicular or deep-seated thyroid nodules should lead to the discontinuation of the procedure and thoracic radiographs should be performed to the patient.

Thromboembolism

Blindness of the right eye has been described in an 81-year woman, immediately after FNB of a mass on the right anterior triangle of the neck³⁴. The mass was of unknown origin, because FNB was cytologically non-diagnostic. The rapidity of the onset of vision loss and the location of the mass at the carotid bifurcation made a traumatic plaque dislodgment or thromboembolism due to the FNB the most possible explanation³⁴. In the literature, there are some cases of cerebral embolism following FNB of the lung^{35,36}. Similarly, thyroid FNB might have been complicated with cerebral embolism, especially in older patients or patients predisposed to thrombophilic conditions. Despite the lack of direct evidence, it is suggested that FNB on thyroid nodules in close vicinity to carotid should be performed under U/S guidance, especially if known carotid artery atherosclerosis coincides. Furthermore, in elderly patients, especially when they are in bad general condition, FNB should be carefully weighed in advance, since the majority of differentiated thyroid carcinomas have slow progress allowing a long-term survival, even if untreated³⁷.

Needle tract seeding of medullary thyroid carcinoma or thyroid lymphoma

Despite the alarming *in vitro* observations, needle track seeding (or tumor dissemination) is very rare *in vivo*. Tumor cells released into the surrounding tissues or circulation after FNB are probably destroyed by the host immune response or other mechanisms before giving rise to clinically apparent metastases⁸. Implantation may be facilitated in cases of immunodeficiency or untreated carcinomas. Post-FNB cutaneous or muscular seedings have been described in papillary (15 cases), follicular (3 cases) and anaplastic thyroid carcinoma (1 case)³⁸.

However, needle tract seeding of medullary thyroid carcinoma (MTC), thyroid lymphoma or other primary thyroid malignancies have not been reported in the literature yet. A possible, albeit hypothetical, explanation is that the patients with MTC are subjected to total thyroidectomy and extensive nodal dissection, shortly after the cytological diagnosis of MTC. Furthermore, patients with residu-

al disease after surgery may be subjected to radiotherapy and/or cytotoxic chemotherapy, which might destroy any potential post-FNB implantation⁷. Similarly, the patients with thyroid lymphoma are subjected to radiotherapy and/or cytotoxic chemotherapy, which might further limit the already minimal risk of needle tract seeding⁷. As in the cases of needle tract seeding of differentiated thyroid carcinoma⁸, we believe that, given the easiness and effectiveness of surgical removal of the seedings, the application of FNB on thyroid nodules should not be deterred, when indicated.

Conclusion

According to our hypothesis, there may be five distinct expected but still unpublished complications following thyroid FNB: cyst fluid leakage, anaphylactic reaction, pneumothorax, thromboembolism and needle tract seeding of MTC or thyroid lymphoma. Cyst fluid leakage and pneumothorax may be of minimal clinical significance. Needle tract seeding of MTC or thyroid lymphoma may not have significant clinical consequences, if someone considers the easiness and effectiveness of surgical removal of needle tract seeding in cases of differentiated thyroid carcinoma. On the contrary, anaphylactic reaction or thromboembolism may be life-threatening. The performers of thyroid FNB are hereby encouraged to publish these complications, if they ever occur, because awareness of them could render FNB even safer.

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