HYPOTHYROIDISM AFTER FINE NEEDLE ASPIRATION BIOPSY OF THYROID NODULES – A CASE REPORT

HIPOTIROIDIZAM KAO POSLEDICA ASPIRACIONE BIOPSIJE TANKOM IGLOM NODUSA ŠTITASTE ŽLEZDE – PRIKAZ SLUČAJA

Jovana PRODANOVIĆ SIMEUNOVIĆ¹, Tijana IČIN¹,², Đorđe POPOVIĆ¹,², Damir BENC¹,², Kristina STEPANOVIĆ¹ and Milica MEDIĆ STOJANOSKA¹,²

Summary

Introduction. Fine needle aspiration biopsy is a non-surgical invasive diagnostic method for the cytological evaluation of the thyroid gland. Complications of fine needle aspiration biopsy are rare. Case Report. A female patient, 64 years of age, underwent left-sided nodulectomy in 2006, due to a follicular adenoma of the thyroid gland. In September of 2016, ultrasonography of the thyroid gland confirmed a node in the right lobe, approximately 10 mm in the longest diameter. The thyroid-stimulating hormone level was within the reference range (1.8 mIU/L), as well as calcitonin and carcinomembranase antigen levels, but with elevated anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies, so fine needle aspiration was indicated. The cytological finding indicated a suspected follicular lesion and total thyroidectomy with an excisional biopsy was proposed in November of 2016. Prior to the surgery, hormone levels were measured and high thyroid-stimulating hormone levels were recorded (79 mIU/L). Further investigation showed low levels of free thyroid hormone concentrations, and levothyroxine was initiated at a dose of 75 mcg per day and the surgical treatment was delayed. The indicated dose of levothyroxine resulted in satisfactory values of the thyroid gland free hormones, and in February 2017, right-sided lobectomy was performed, whereas the histopathological findings indicated lymphocytic thyroiditis. Levothyroxine replacement therapy showed satisfactory results in the postoperative period. Further outpatient ultrasonographic monitoring showed a residual thyroid tissue, with slightly non-homogeneous echostucture in the left thyroid bed, 12 x 11 x 32 mm in size. Regular follow-up was suggested. Conclusion. Hypothyroidism has not been reported as a fine needle aspiration complication in the available literature.

Key words: Hypothyroidism; Biopsy, Fine-Needle; Thyroid Nodule; Thyroid Gland; Diagnosis; Ultrasonography; Morphological and Microscopic Findings; Postoperative Complications

Introduction

Thyroid gland nodules are common clinical findings. Fine needle aspiration (FNA) is a non-surgical invasive diagnostic method for the cytological evaluation of the thyroid gland. Complications of FNA are rare. To the best of our knowledge, this is the first report of hypothyroidism, most likely being the consequence of the FNA procedure.

Sažetak

Uvod. Ultrasonografski kontrolisana aspiraciona biopsija tankom iglom – fine needle aspiration nehrirška je invazivna dijagnostička metoda za citološku evaluaciju nodusa štitaste žlezde. Komplikacije pri ovoj biopsiji su retke. Prikaz slučaja. Bolesnica, stara 64 godine, operisana je 2006. godine zbog folikularnog ademona štitaste žlezde u predelu levog režnja, kada je urađena levostrana nodulektomija. U septembru 2016. godine ultrasonografskim pregledom je verifikovan nodus u desnom režnju štitaste žlezde najvećeg promera 10 mm, a vrednost tirostimuliućeg hormona (1,8 mIU/L) u okviru referentnih vrednosti kao i vrednosti kalcitonina i karcinomembranalnog antitela, uz povišene vrednosti antitela na tiroksin peroxidazu i antištitalni linskih antitela, te je indikovana biopsija. Citološki nalaz ukazivao je na suspektnu folikularnu leziju; predložena je totalna tiroidektomija sa biopsijom eks tempore u februaru 2017. godine. Pre operacije kontrolisane su vrednosti hormona, kada su registrovane visoke vrednosti tirostimuliućeg hormona (79 mIU/L), uz niske vrednosti slobodnih hormona štitaste žlezde, te uvećana supstitucija levotiroksinom u dozi od 75 mcg dnevno i odloženo operativno lečenje do normalizacije hormonskog statusa štitaste žlezde kodlicišan je u više navrata; navedena doza levotiroksina dovela je do zadovoljavajućih vrednosti slobodnih hormona štitaste žlezde, te je u februaru 2017. godine bolesnici urađena dobro učinkovita lobektomija, a patohistološki nalaz ukazivao je na limfocitni tiroiditis. Postoperativno, vrednosti hormona štitaste žlezde na dosadašnjoj terapiji ukazuju na zadovoljavajuću supstituciju levotiroksinom. U daljem ambulantnom praćenju ultrasonografski potvrđeno je postojanje rezidualnog tkiva štitaste žlezde u loži levog režnja. U odnosu na antitela imaju normale vrednosti, a koncentracije tirostimuliućeg hormona u dozi 12 x 11 x 32 mm. Predloženo je dalje praćenje. Zaključak. Hipotiroidizam do sada nije opisan u literaturi kao komplikacija nakon biopsije tankom iglom. Ključne reči: hipotiroidizam; aspiraciona biopsija tankom iglom; tireoidni čvor; štitna žlezda; dijagnoza; ultrasonografska; morfološki i mikroskopski nalazi; postoperativne komplikacije.
Case Report

A female patient, 64 years of age, presented with a nodule in the area of the left lobe of the thyroid gland in 2005. Thyroid-stimulating hormone (TSH) and free thyroid hormone levels were in the reference range, with high antithyroid antibody titer. She underwent left-sided nodulectomy in 2006, due to a follicular adenoma of the thyroid gland in the left lobe region. Annual ultrasound check-ups and TSH level measurements were conducted. In September of 2016, ultrasonography of the thyroid gland confirmed a hypoechoic nodule in the right lobe of thyroid gland, 6 x 10 mm, anteroposterior (AP) x craniocaudal (CC) in size (Figure 1). The patient was afraid of having a malignant disease. At that time, the TSH level was within the reference range (1,8 mIU/L) as well as calcitonin and carinoembryonic antigen (CEA) levels, but with elevated antibodies to thyroid peroxidase (TPO) and antithyroglobulin (TG). The cytological finding indicated a suspected follicular lesion and total thyroidectomy with an ex tempore biopsy was proposed in November of 2016. Prior to the surgery, thyroid hormones checkup was performed and high TSH levels were recorded (79 mIU/L) (Table 1), as well as low values of free thyroid hormones.

Thyroid ultrasonography was performed and hypothyroidism was established, but no morphological changes were registered. Levothyroxine replacement therapy, at a dose of 75 mcg per day, was initiated and the surgical treatment was delayed. The patient denied pain, swollen neck, or any other illness after FNA. The indicated dose of levothyroxine resulted in satisfactory levels of the thyroid gland free hormones, and in February 2017, the patient underwent right-sided lobectomy; the histopathological findings indicated lymphocytic thyroiditis. The postoperative thyroid hormone levels in the previous therapy indicated satisfactory substitution with levothyroxine. Further outpatient ultrasound monitoring showed a residual thyroid tissue in the left lobe, 12 x 11 x 32 mm in size, with slightly non-homogeneous echostucture. Further follow-up was suggested.

Discussion

Therapeutic punctures of the thyroid gland used to be performed using instruments that resemble modern aspiration needles, first described in the famous research of Kitab at-Tasrif (The Method of Medicine), the most influential book of Arabic medieval medicine.

Table 1. Nodules in the right lobe of the thyroid gland

| Nodus u predelu desnog režnja štitaste žlezde |
|---------------------------------------------|
| Figure 1. Nodule in the right lobe of the thyroid gland |

His description resembles the modern FNA biopsy of the thyroid gland [1]. Since 1994, many studies have evaluated the efficacy and safety of FNA, so the use of FNA has rapidly increased at the beginning of 2010 [2]. FNA plays a central role in the assessment of the malignant nature of the thyroid gland nodules. FNA biopsy should be selective, since systemic FNA of all nodules, regardless of size or appearance, is superfluous and even leads to unnecessary invasive diagnosis. Quick diagnosis can mean early detection of cancer, giving more options for treatment, and diagnosing benign nodules can reduce the number of unnecessary surgeries [3]. Medical history data and ultrasonographic characteristics of nodules are used in deciding whether FNA biopsy is necessary. In our case report, the ultrasonographic properties of the nodules did not require FNA to be done immediately, but it was nevertheless indicated, since the nodules were not verified at previous ultrasound controls and because the patient expressed fear of a potentially malignant disease. Complications related to blood extravasation are more common in patients with a deep lesion or when the lesion has a cystic component that is > 50% of the overall size of the lesion. The risk is slightly higher in cystic compared to solid nodules. The most common manifestation of bleeding is local pain, mild dysphagia (probably the result of unintentional esophageal puncture), and sometimes visible local edema. Acute or delayed diffuse swelling of the thyroid gland, after which in some cases patients need corticosteroid therapy, is rarely associated with compromised airways. There may also be paralysis of recurrent laryngeal nerves, cervical radiculopathy [4]. Our patient denied pain or edema after FNA, and they probably have not occurred. One study showed post aspiration thyrotoxicosis that occurred in 1% of patients, and the origin is unknown.

In our case, there is a possibility that the patient had a sub-clinical post-aspiration thyrotoxicosis that was not confirmed due to the lack of clinical symp-
toms. Other rare complications that are the subject of several case reports include the development of fibrovascular tumors, such as hemangiomata or pseudoaneurysm [4].

If our patient had these complications, they would be histopathologically confirmed, but these findings indicated lymphocytic thyroiditis.

Fine needle aspiration can also destroy thyroid gland follicles, which leads to the release of TG into the circulation. Leakage of fluid from the cystic nodes to the surrounding thyroid tissue (perinodular) or other tissues close to the thyroid gland (perithyroid) is a potential post-FNA complication, which may cause acute thyroiditis. Mild thyroiditis and/or subsequent fibrosis of the thyroid tissue should not be excluded. In our patient, the thyroid gland had no cystic component. Hypothyroidism may have occurred as a result of subacute thyroiditis that was not verified after FNA, but the absence of neck pain makes it less likely, and thyroid tissue fibrosis has not been proven histopathologically. Leakage of ethanol is described after percutaneous injection of ethanol (usually through a thin needle under ultrasound guidance), which is a therapeutic method for cystic degeneration of nodules.

Ethanol leakage may cause local pain and fibrosis in the surrounding tissues, which is caused by an increase in intranodal pressure after ethanol injection. Usage of local anesthetics, especially lidocaine, or parasitic cyst rupture, may cause an anaphylactic reaction.

Local anesthetics are used only prior to FNA in some patients. Cases of thyroid gland cysiceriosis are also reported, but these are usually cases with the involvement of the thyroid gland in generalized cysiceriosis. However, other parasitic cysts might more easily be mistaken for simple thyroid cystic nodules, because their primary lesion may be in the thyroid gland. Primary hydatid cysts of the thyroid gland caused by echinococcosis, although rare, have been reported, and its dissemination may be a potential complication. Our patient did not have a cystic component, and local anesthetics were not used. Thyroid FNA may be complicated with cerebral embolism, especially in elderly patients or patients predisposed to thrombophilic conditions. Blindness was described as a consequence of thromboembolism in one patient. Despite the lack of direct evidence, it is recommended that thyroid FNA of nodules in the immediate vicinity of the carotid artery should be performed under ultrasound control, especially if there is evidence of carotid artery atherosclerosis. In our patient, FNA was performed under ultrasound control. Thromboembolism of the thyroid artery may cause sudden hypothyroidism, but this would lead to ischemia of the thyroid gland tissue that should have been verified by an ultrasound examination which is done when hypothyroidism is diagnosed or post-surgical finding is established. Malignant scarring after FNA is rarely described, but most often in medullar carcinoma of the thyroid gland or thyroid lymphoma, and extremely rare in other malignant thyroid diseases [5, 6]. In our patient, malignant cell scattering was not possible, since it was not a malignant thyroid disease. A case of a 35-year-old woman who was admitted to the hospital after a three-day vocal roughness, laryngeal stridor and dyspnea without fever, was reported after FNA was performed, which was confirmed with retropharyngeal cellulitis [7, 8]. A 35-year-old man was examined because of painless edema, which gradually increased on the right side of the neck after FNA. He had no symptoms of thyroid function disorder, no obstructive symptoms and no history of chronic disease or surgery. He was diagnosed with abscess in the area of the right thyroid gland. Thyroid abscess and acute suppurative thyroiditis have been described as rare complications of thyroid FNA. A transition phase of hyperthyroidism has also been reported due to the secretion of thyroid gland hormone in connection with mass destruction of tissue associated with abscess [9]. The medical history of our patient and a histopathological examination showed no data indicating the existence of cellulitis, abscess or other purulent infection. Hashimoto thyroiditis is part of the spectrum of autoimmune thyroid disease and is characterized by the destruction of thyroid cells by various cell and antibody induced immune processes. This condition is the most common

### Table 1. Levels of the thyroid-stimulating hormone, free T3, free T4 levels before and after fine needle aspiration, as well as before and after surgery

| TSH (mIU/l) | Free T4 (pmol/l) | Free T3 (pmol/l) |
|------------|-----------------|-----------------|
| Level before FNA/Vrednost pre FNA | 1,8 | 14,4 | 4,26 |
| Level after FNA/Vrednost nakon FNA | 79 | 5,3 | 2,4 |
| Level before surgery (levothyroxine 75 mcg/day) | 2,8 | 16,2 | 4,70 |
| Vrednost pre operacije (levotiroksin 75 mcg/dan) | | | |
| Level after surgery (levothyroxine 75 mcg/day) | 4,2 | 19,9 | / |
| Vrednost posle operacije (levotiroksin 75 mcg/dan) | | | |

Legend: FNA – fine needle aspiration; TSH – thyroid-stimulating hormone; T3 – triiodothyronine; T4 – thyroxine

Vrednosti tireostimulišućeg hormona, slobodnog T3, slobodnog T4 pre i nakon FNA, kao i pre i nakon operacije

Tabela 1. Vrednosti tireostimulišućeg hormona, slobodnog T3, slobodnog T4 pre i nakon FNA, kao i pre i nakon operacije
cause of hypothyroidism [3, 10–12]. Although our patient had Hashimoto thyroiditis for more than 10 years, TSH values during regular controls were normal and the absence of symptoms of hypothyroidism indicated a still preserved function of the thyroid gland before performing FNA. Considering that hypothyroidism in our patient has progressed rapidly, within a period of two months after FNA, in our opinion hypothyroidism was not the result of autoimmune thyroiditis alone, most likely the consequence of the FNA procedure itself.

**Conclusion**

Hypothyroidism has not been described in literature as a complication after fine needle aspiration. The medical history, surgery and histopathological findings after surgery did not clarify the etiology of the sudden development of hypothyroidism in our patient. We seriously consider that the cause of hypothyroidism was fine needle aspiration. According to guides, routine control of thyroid hormone status after fine needle aspiration is not indicated.

**References**

1. Abu al-Qasim al-Zahrawi (Abulcasis). The Kitab al-Tasrif (The Method of Medicine).
2. Ha EJ, Suh CH, Baek JH. Complications following ultrasound-guided core needle biopsy of thyroid nodules: a systematic review and meta-analysis. Eur Radiol. 2018;28(9):3848-60.
3. https://www.myvmc.com/investigations/fine-needle-aspiration-biopsy-fna/ [assessed 27 Jan 2019].
4. https://www.insideradiology.com.au/thyroid-fna-hp/ [assessed 27 Jan 2019].
5. Polyzos SA, Anastasilakis AD. Clinical complications following thyroid fine-needle biopsy: a systematic review. Clin Endocrinol (Oxf). 2009;71(2):157-65.
6. Polyzos SA, Anastasilakis AD. Rare potential complications of thyroid fine needle biopsy. Hippokratia. 2011;15(2):116-9.
7. Sato K, Izumi T, Toshima M, Nagai T, Muroi K, Komesu N, et al. Retropharyngeal abscess due to methicillin-resistant Staphylococcus aureus in a case of acute myeloid leukemia. Intern Med. 2005;44(4):346-9. Rad je primljen 28. I 2019. Recenziran 3. II 2019. Prihvaćen za štampu 4. II 2019. BIBLID.0025-8105:(2019):LXXII:1-2:43-46.
8. Cesareo R, Naciu A, Barberi A, Pasqualini V, Pelle G, Manfrini S, et al. A rare and severe complication following thyroid fine needle aspiration: retropharyngeal cellulitis. Int J Endocrinol Metab. 2016;14(4):e39174.
9. Mohamed AAR, Al Quarshi TA, Mohamed AA, Saud AMA. Thyroid abscess rare complication of thyroid FNA: case report and literature review. Sch J Med Case Rep. 2018;6(2):101-7.
10. Dilas LT, Bajkin I, Icin T, Paro JN, Zavisic BK. Iodine and thyroid gland with or without nuclear catastrophe. Med Pregl. 2012;65(11-12):489-95.
11. Dilas LT, Icin T, Paro JN, Bajkin I. Autoimmune thyroid disease and other non-endocrine autoimmune diseases. Med Pregl. 2011;64(3-4):183-7.
12. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. Autoimmun Rev. 2014;13(4-5):391-7.