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Case Report

Complexity of diagnosis and management of a giant thyroid nodule: A case report and a concise literature

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Abstract

It is crucial for doctors to decide whether a thyroid nodule is benign or malignant when a patient presents with one, as it will significantly impact how the patient is managed in the future. However, it is not as straightforward to determine between the two; even a physical examination, thyroid function test, ultrasonography, and biopsy have been well performed. It can be more stressful if a patient has an increased risk of malignancy, such as age (below 20- and above 60-year-old), solid nodule, rapid growth, hoarseness, lymphadenopathy, and microcalcifications on the ultrasonography. The aim of this case was to present the management of a giant thyroid nodule with malignancy presentation and a benign biopsy finding. A 41-year-old male complained of a palpable neck mass, hoarseness, and dysphagia. The thyroid function test was normal. Ultrasonography revealed suspicion of malignancy with category 4 of American College of Radiology-Thyroid Imaging Reporting and Data System (ACR-TIRADS). The biopsy revealed follicular neoplasm, and was classified as Bethesda IV. The patient underwent a total thyroidectomy due to the large tumor size and symptoms. Histopathological findings post-surgery revealed a follicular thyroid adenoma. This case highlights a complex diagnosis and management of follicular thyroid neoplasm due to their potential for both benign and malignant. Comprehensive pre- and post-operative care is essential to determine the nature of nodules. Post-operative follow-up care might improve the patient's outcome and prevent complications.

Keywords: Follicular neoplasm, follicular thyroid cancer, follicular thyroid adenoma, thyroidectomy, thyroid carcinoma

Introduction

A giant thyroid nodule is defined as a nodule larger than four centimeters [1]. When a patient presents with a thyroid nodule, physicians should determine whether it is benign or malignant, as this will significantly impact future patient care. However, it is not as simple to distinguish between the two, even after a thorough physical examination, thyroid function test, ultrasonography, and biopsy. Management in patients with risk factors for malignancy, such as age (below 20- and above 60-years-old), solid nodule, rapid development, hoarseness, lymphadenopathy, and ultrasonographic microcalcifications [2], can be more stressful. While

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Received: May 25, 2023 - Accepted: September 20, 2023 - Published online: October 16, 2023

benign thyroid neoplasm contributes to 95% of thyroid nodules, 2% of thyroid malignancies arise within benign thyroid nodules [3]. Thyroid cancer increased from 7.1 to 17.6 per 100,000 in the past 13 years and this trend is largely attributed to improved diagnostic tests [4].

Thyroid ultrasonography and fine needle aspiration cytology (FNAC) can be used to determine whether or not a thyroid nodule has malignant characteristics. Based on ultrasonography, the five-category system (TR1 to TR5) from the American College of Radiology-Thyroid Imaging Reporting & Data System (ACR-TIRADS) can be employed [5]. TR1, TR2, and TR3 pose a low risk of malignancy, whereas TR4 and TR5 suggest malignancy, necessitating FNAC. FNAC results are reported using the Bethesda system, which includes the following six categories: I: nondiagnostic, II: benign, III: atypia of undetermined significance, IV: follicular neoplasm, V: suspicious for malignancy, and VI: malignant. For individuals with Bethesda IV category (follicular neoplasm), the risk of malignancy is 50% (28–100%) [6]; therefore, surgical resection is necessary so that a thorough histopathology slide resection can be performed, and a histopathology diagnosis can be made after a complete nodule or thyroid gland specimen is evaluated.

Because follicular thyroid neoplasms can be benign (adenoma) or malignant (carcinoma), comprehensive pre-and post-operative care might help to ensure optimal patient outcomes and prognosis, especially in patients with high suspicion of malignancy. Management of follicular thyroid adenoma is far different from follicular thyroid carcinoma. Post-operative follow-up care might prevent the recurrence of thyroid carcinoma. Close monitoring of thyroid hormone levels and promptly addressing any signs of potential complications or disease progression will lead to better long-term patient management and quality of life. In this case report we present the management (including the pre- and post-operative management) of a giant thyroid nodule with malignancy presentation and a benign biopsy finding (follicular neoplasm).

Case

A 41-year-old male patient presented to Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia with a palpable mass in the neck for the past two years, accompanied by dysphagia, hoarseness, and significant weight loss of 16 kg over the last three months. The mass gradually increased in size without any associated pain.

The patient was underweight (BMI 18.1 kg/m^2), and the vital sign examination showed no remarkable findings. Clinical examination revealed a solid mass in the neck, 8x2 cm on the right thyroid lobe, 3x1 cm in the middle, and 5x2 cm on the left lobe with solid consistency and no pain upon palpation (**Figure 1A**). FNAC revealed a follicular neoplasm of the thyroid gland, which was classified as Bethesda IV with a 10–40% risk of malignancy [7]. Other physical examinations were within normal range.

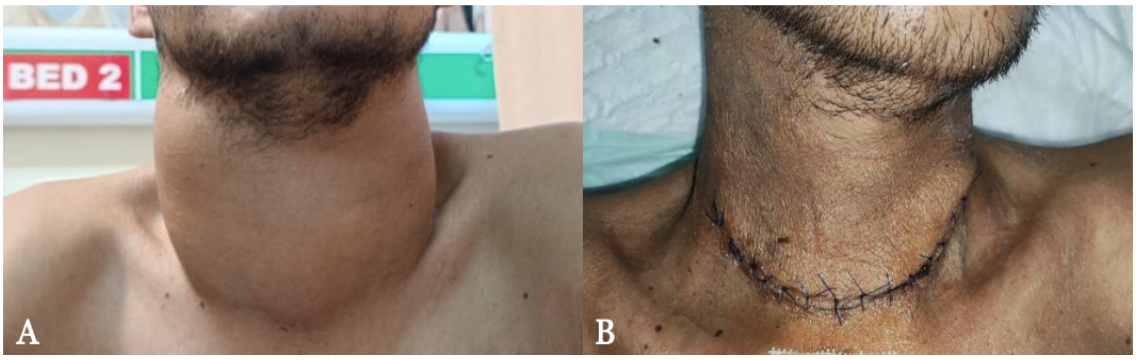

Figure 1. Clinical photos of the patient pre-surgery (A) and post-surgery (B).

Laboratory showed normal thyroid function with FT4 was 16.08 (reference 9–20) pmol/L, thyroid stimulating hormone (TSH) was 1.38 (0.25–5) mlU/L, calcium was 9.0 (8.6–10.3) mg/dL, and albumin was 8.9 (3.5–5.2) g/dL. A laryngeal computed tomography scan (CT scan) revealed a large lobulated mass with multiple areas of calcification and necrosis that filled the right thyroid gland, extended into adjacent structures, including the oropharynx and

intrathoracic larynx, and pushed against the trachea (**Figure 2**). Multiple lymphadenopathies less than 1 cm in size were seen in the right and left paracervical. The compression resulted in dysphagia and necessitated a gastrostomy tube for feeding. The following recommended step was molecular testing (gene mutation assay), which was not conducted due to a lack of facility.

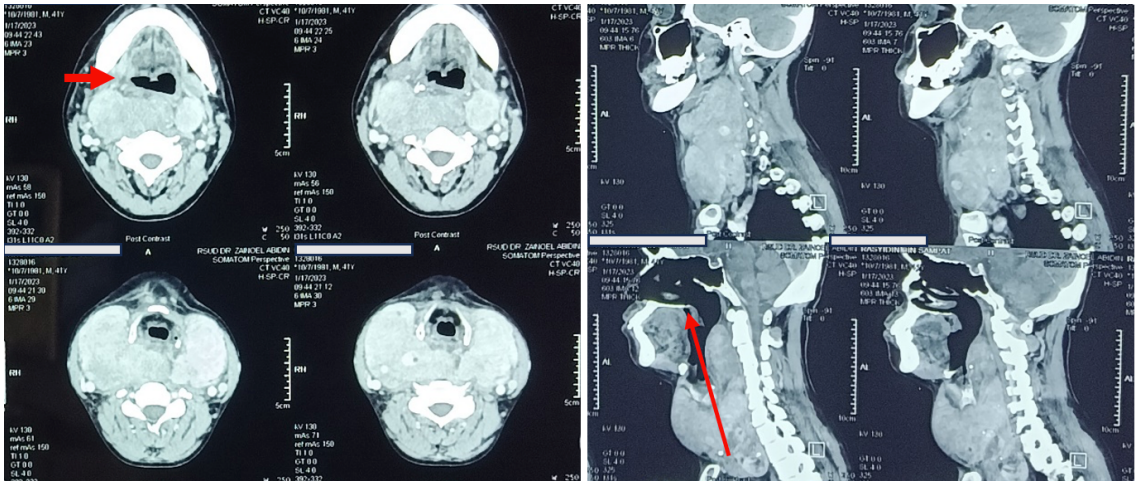

Figure 1. Contrast-enhanced CT-scan showed lobulated solid masses that contained multiple calcifications and necrotic areas that filled the right and left thyroid lobes. It compresses on the trachea (short red arrow). It causes trachea narrowing to the right in the axial plane, and extends to the oropharynx, pharynx, and intrathoracic (VC2 - VTh2) in the sagittal plane (long red arrow).

Considering the patient tumor size and pressure on the surrounding organs, the patient underwent a total thyroidectomy (**Figure 1B**). The thyroid nodule after total thyroidectomy is presented **Figure 3**. Histopathological examination post-surgery revealed a follicular thyroid adenoma, confirming a benign tumor. Thyroid function after surgery was normal, with FT4 10.67 pmol/L and TSH 2.47 mIU/L. Four weeks after surgery, the patient was prescribed levothyroxine 100 mg once a day and calcitriol 0.5 mg twice a day and would be continued long-life as replacement therapy.

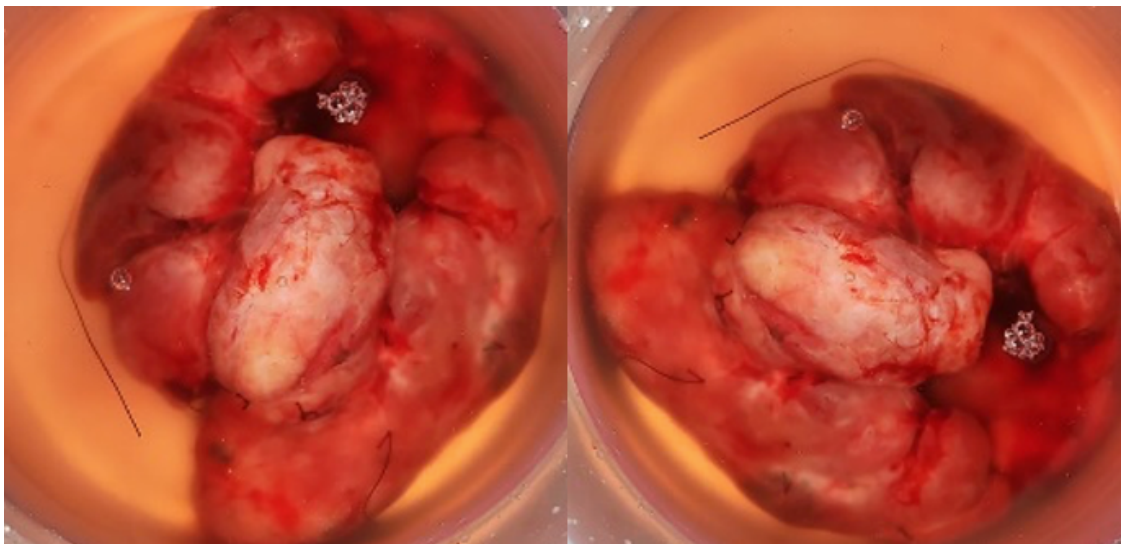

Figure 3. Giant thyroid nodule after total thyroidectomy.

Discussion

Follicular thyroid neoplasms (follicular adenoma and follicular carcinoma) exhibit numerous clinical and cytological similarities, posing challenges in distinguishing between benign and malignant thyroid nodules or achieving an accurate preoperative diagnosis [8,9]. The most common feature of thyroid neoplasm is neck swelling and more concern should be given to the

patient with the sudden enlargement of the neck mass with some symptoms like hoarseness, dysphagia, or shortness of breath due to the pressure of the nodule on the surrounding structures [10]. Our patient had a gradual increase in neck mass and dysphagia on admission, resulting in malnutrition and weight loss.

TSH measurement and thyroid ultrasonography are recommended for patients with thyroid nodules. For patients with low TSH levels and hyperthyroidism, a ^{123}I thyroid scan is recommended to determine the cause of hyperthyroidism. In this case, the TSH level was normal; therefore, the ^{123}I scan was not performed. Those with normal or elevated TSH levels should proceed to thyroid ultrasonography and consider FNAC (**Figure 4**) if there are suspicious features on ultrasonography examination [11].

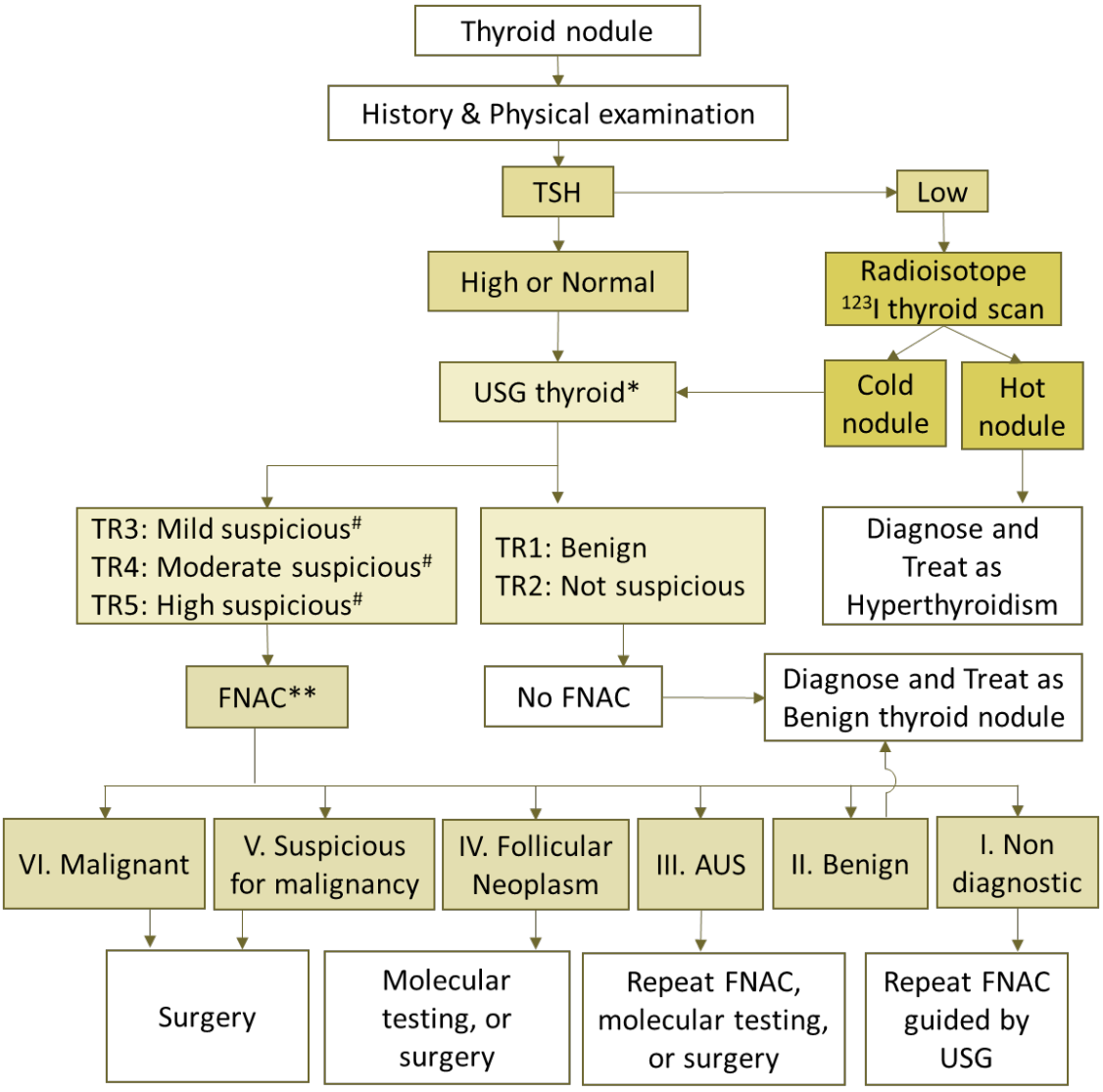

Figure 4. Algorithm of thyroid nodule diagnosis and management [5,10]. FNAC: fine needle aspiration cytology; AUS: atypia of underestimated significance. Notes: # based on size threshold of FNAC; * based on TI-RADS classification; and *** based on Bethesda system.

Thyroid ultrasonography may predict malignancy in nodules with high sensitivity (90%) and specificity (91.1%) [12]. Five categories of ACR-TIRADS are commonly used to stratify the likelihood of malignancy. This classification is based on five factors: nodule composition, echogenicity, shape, margins, and echogenic focus [5]. Each component has a value, resulting in stratification from TR1 to TR5. TR1 is benign, TR2 is not suspicious, and FNAC is not required; TR3 is mildly suspicious and FNAC is recommended if the nodule size is ≥2.5 cm; TR4 is

moderately suspicious and FNAC is warranted if the nodule size is ≥1.5 cm; and TR5 is highly suspicious and FNAC is needed if the nodule size is ≥1 cm [5].

Available guidelines have suggested several criteria for the FNAC procedure. American Thyroid Association recommends using the Bethesda system for reporting thyroid cytopathology to stratify the FNAC results [10]. It ranges from I (benign) to VI (malignant). Follicular neoplasm, as category IV, has several follicular-patterned lesions, including follicular nodular disease, follicular adenoma, invasive follicular variants of papillary thyroid carcinoma, follicular thyroid carcinoma, and non-invasive follicular thyroid neoplasm with papillary-like nuclear features [13]. The National Comprehensive Cancer Network also recommends FNAC as the primary test, followed by thyroid ultrasonography if not previously done, and CT scan or magnetic resonance imaging as the follow-up diagnostic procedure [11].

A CT scan is not frequently used in the management of thyroid nodules. However, a CT scan was performed in this case due to its large size, as a CT scan may supplement neck ultrasonography for detecting involvement of the surrounding structure and the potential of macrometastases in the central compartment, mediastinum, and behind the trachea [10].

Surgery enables a definitive diagnosis of nodules with malignant potential (Bethesda III-VI). Lobectomy is advised for disorders that affect only one lobe. A near-total thyroidectomy should be considered if a nodular goiter is detected. In benign lesions (Bethesda II), even if asymptomatic, surgical may be considered if nodules >4 cm due to increased risk of malignancy and potential false negative FNAC, symptomatic nodules such as dysphagia or airway obstruction, cosmetic concern, and retro-clavicular and mediastinal extension [14].

Molecular testing (if available) should be performed before surgery. In the treatment of Bethesda IV thyroid nodules, molecular testing is necessary as it can help distinguish benign from malignant lesions, serve as a guide for surgical intervention (high-risk nodules will need a more extensive surgical procedure, such as a total thyroidectomy), and avoid unnecessary surgery (low-risk nodule can be managed by active surveillance). The tests that are typically employed include gene mutation assays for *BRAF*, *RAS*, and *RET/PTC* rearrangements [10].

Histopathology examination is the first step in the management of post-operative thyroid nodules. Since distinguishing benign from malignant follicular thyroid nodules before surgery has been a challenging diagnostic issue, post-operative confirmation of follicular carcinoma usually relies on histopathological examination to detect capsular or vascular invasion [8].

Risk stratification should be done based on the cytology results following histopathological results. Individuals with benign cytology results will have levothyroxine supplementation with a normal range of TSH targets. If the cytology reveals carcinoma (papillary thyroid carcinoma or follicular thyroid carcinoma), the next step is to do a risk stratification (**Figure 5**). American Thyroid Association recommends radioiodine therapy if there are distant metastases, extrathyroidal extension, or tumor size above four cm [10]. National Comprehensive Cancer Network suggests lobectomy and isthmusectomy unless invasive or metastatic cancer is detected, followed by radioiodine whenever possible [11].

This patient was in a euthyroid state prior to surgery. The thyroid nodule was larger than 4 cm. The laryngeal CT scan revealed a concerning nodule, and the FNAC showed a follicular neoplasm classified as Bethesda category IV. Based on these findings, the patient underwent total thyroidectomy, which was carried out successfully.

Levothyroxine is the mainstay hormone replacement therapy after total thyroidectomy, with a target of a normal range of TSH for those with benign cytology findings. For individuals with malignancy, the purpose of levothyroxine is not only as supplementation but also to suppress the production of TSH from the pituitary gland. After the initial surgery, patients with thyroid carcinoma in the American Thyroid Association high- and intermediate-risk category should be maintained at TSH below 0.1 mIU/L and between 0.1 mIU/L to 0.5 mIU/L for low-risk [10,11,15]. In our case, the histopathologic finding post-total thyroidectomy was a follicular thyroid adenoma. The patient was then treated with levothyroxine with the target of TSH level within normal range. Follicular thyroid adenoma has a good prognosis, even follicular thyroid carcinoma has a five-year survival rate (98.1%), with a great reduction to 39.3% if metastasis occurs.

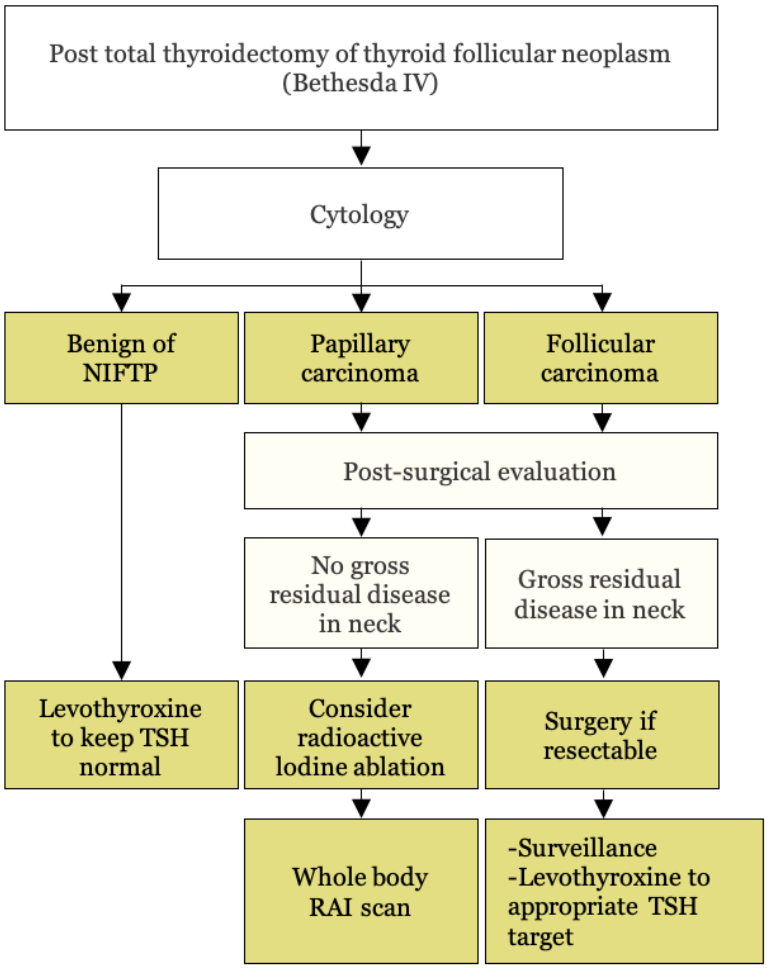

Figure 5. National Comprehensive Cancer Network algorithm of follicular thyroid neoplasm [11]. NIFTP: Noninvasive follicular thyroid neoplasm with papillary-like nuclear features.

Conclusion

This case report highlights the challenges in diagnosing and managing giant thyroid nodules, especially a follicular thyroid neoplasm. TSH measurement and thyroid ultrasonography are the initial approach, then followed by FNAC based on ultrasonography findings. Postoperative management, a histopathology examination is crucial in confirming the malignancy, followed by a levothyroxine prescription and risk stratification for thyroid malignancy.

Ethics approval

The patient provided written informed consent to be published as a case report.

Competing interests

The authors declare that there is no conflict of interest.

Acknowledgments

We would like to express our gratitude to patient and family.

Funding

This study received no external funding.

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

How to cite

Firdausa S, Zufry H, Ekadamayanti AS, *et al*. Complexity of diagnosis and management of a giant thyroid nodule: A case report and a concise literature. Narra J 2023; 3 (3): e224 - http://doi.org/10.52225/narra.v3i3.224.

References

1. Karagöz ZK, Doğan S, Kurt F, *et al*. Is fine needle aspiration biopsy effective in detecting malignancy in giant thyroid nodules? East J Med 2023;28(2):301-306.
2. Perros P, Boelaert K, Colley S, *et al*. Guidelines for the management of thyroid cancer. Clin Endocrinol 2014;81 Suppl 1:1-122.
3. Arora N, Scognamiglio T, Zhu B, *et al*. Do benign thyroid nodules have malignant potential? An evidence-based review. World J Surg 2008;32(7):1237-1246.
4. Olson E, Wintheiser G, Wolfe KM, *et al*. Epidemiology of thyroid cancer: A review of the national cancer database, 2000-2013. Cureus 2019;11(2):e4127.
5. Tessler FN, Middleton WD, Grant EG, *et al*. ACR thyroid imaging, reporting and data system (TI-RADS): White paper of the ACR TI-RADS committee. J Am Coll Radiol 2017;14(5):587-595.
6. Baloch Z, Cooper D, Schlumberger M, *et al*. Overview of diagnostic terminology and reporting. In: The Bethesda system for reporting thyroid cytopathology. 3rd edn. Edited by Ali SZ, VanderLaan PA. Switzerland: Springer Cham; 2023:1-10.
7. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. Thyroid 2017;27(11):1341-1346.
8. Kuo TC, Wu MH, Chen KY, *et al*. Ultrasonographic features for differentiating follicular thyroid carcinoma and follicular adenoma. Asian J Surg 2020;43(1):339-346.
9. McHenry CR, Phitayakorn R. Follicular adenoma and carcinoma of the thyroid gland. Oncologist 2011;16(5):585-593.
10. Haugen BR, Alexander EK, Bible KC, *et al*. 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 2016;26(1):1-133.
11. Haddad RI, Bischoff L, Ball D, *et al*. Thyroid carcinoma, version 2.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2022;20(8):925-951.
12. Kundi S, Jabeen M, Rafique MS, *et al*. Validity of thyroid ultrasound in diagnosing malignancy in thyroid nodule. Pak J Med Health Sci 2022;16(02):32-32.
13. Auger M, Callegari F, Fadda G, *et al*. Follicular neoplasm. In: The bethesda system for reporting thyroid cytopathology. 3rd edn. Edited by Ali SZ, VanderLaan PA. Switzerland: Springer Cham; 2023.
14. Durante C, Hegedüs L, Czarniecka A, *et al*. 2023 European thyroid association clinical practice guidelines for thyroid nodule management. Eur Thyroid J 2023;12(5):e230067.
15. Pacini F, Basolo F, Bellantone R, *et al*. Italian consensus on diagnosis and treatment of differentiated thyroid cancer: joint statements of six Italian societies. J Endocrinol Invest 2018;41(7):849-876.