Massive Calcification in a Giant Nodular Thyroid Disease: A Case Study and Review of the Literature

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Abstract: A thyroid nodule is characterized as a discrete lesion, distinguishable from the adjacent thyroid parenchyma, and is frequently encountered in clinical settings. Currently, the terminology "nodular disease of the thyroid" is advised for use in both clinical and pathological classifications due to its expansiveness. Individuals with longstanding multinodular goitres are at risk for cystic degeneration, haemorrhaging, and dystrophic calcification. The main aim of this report is to assess the potential risk of cancer, mitigate the chances of obstructive symptoms and formulate a strategy for a secure and efficient surgical procedure. This paper presents a case involving a 68-year-old female patient who reported an anterior neck mass persisting for 35 years. Clinical assessments, imaging studies, and pathological examinations indicated extensive calcification within a giant nodular thyroid disease, which exerted pressure on the colloid goitre, reducing it to a thin peripheral layer without atypical features. The distinct contribution of this case is the emphasis on the uncommon nature of this presentation, and the associated diagnostic uncertainty, despite the presence of extensive macrocalcification, which still raises concerns about malignancy and necessitates thorough examination. Additionally, it underscores the notable surgical difficulties posed by the density, size, and potential adherence of the calcified tissue to adjacent structures. Key clinical insights reveal that imaging plays a vital role in surgical planning, that the prevention or alleviation of symptoms is an important outcome and that histopathological analysis remains the gold standard for diagnosis. The occurrence of extensive calcification in such a condition is uncommon. Effective collaboration among clinicians, radiologists, and pathologists is essential for accurate diagnosis and informed decision-making regarding thyroid nodular disease. Early diagnosis and intervention for nodular thyroid conditions are advocated, as advancing lesions may lead to compressive complications.

Keywords: Thyroid nodule, giant, calcification, colloid goitre, neck radiograph, anterosternal, retrosternal, surgery.

INTRODUCTION

A thyroid nodule (TN) is characterized as a lesion that is distinct from the surrounding thyroid parenchyma [1]. These nodules are frequently encountered in clinical settings [2]. When nodules are observed in one or more regions of the thyroid, the condition is termed nodular goitre. Conversely, the presence of a single nodule is referred to as a solitary thyroid nodule (STN) [1]. Currently, the classification of thyroid conditions is recommended to employ the term nodular disease of the thyroid, as it offers a more comprehensive descriptor than TN [3]. The thyroid gland, named “thyreoeides” (from Greek, meaning shield-shaped), was first attributed to Thomas Wharton in his work Adenographia in 1656 [4]. Although thyroid nodules are often identified in clinical practice, they can present significant diagnostic challenges [2,5]. Giant thyroid nodules, generally characterised by a diameter exceeding 4cm, represent a specific category within the broader classification of thyroid nodules. Consequently, they share similar epidemiological risk factors with their smaller counterpart. However, these large nodules are relatively rare compared to the overall prevalence of thyroid nodules with a higher rate of compressive symptoms and a higher risk of false negative biopsy result [2].Globally, nodular diseases of the thyroid affect approximately 3-7% of the population, with detection rates varying from 4-7% through physical examination to 19-68% via high-resolution ultrasound scan (USS) [1,6]. Within these ultrasonic examinations, calcifications in the thyroid are frequently observed, with a reported prevalence ranging from 14-55% [7,8]. Long-standing multinodular goitres may lead to cystic degeneration accompanied by haemorrhage, which can subsequently result in dystrophic calcification [9]. In rare cases, large calcified TNs may cause tracheal deviation, contributing to compressive symptoms, and some nodules may extend into the tissue plane between the strap muscles [9]. The primary objective of TN evaluation is to ascertain whether a nodule is benign or malignant. Given the superficial position of the thyroid gland, it is particularly amenable to assessment through ultrasound [6]. In clinical practice, a definitive diagnosis is typically achieved via fine needle aspiration biopsy (FNAB) or surgical

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intervention [10]. Surgical procedures are warranted for nodules that induce respiratory or swallowing difficulties due to compression, or for cosmetic concerns [11]. The prognosis for benign TNs is generally favourable, whereas the outcomes for malignant nodules can vary significantly based on the specific type of cancer [8]. This paper presents a case involving a 68-year-old woman with extensive calcified colloid nodular disease of the thyroid, located in the anterosternal and retrosternal regions and displacing the trachea, resulting in a notable rightward tracheal deviation. This case underscores the positive outcomes associated with surgical intervention and emphasizes the importance of early detection and treatment, as advancing disease may lead to compressive symptoms.

Case Report

A 68-year-old female patient presented in January 2025 with an anterior neck mass that had been evident for the previous 35 years. Initially, a relative observed the swelling, which was approximately the size of her thumb. The mass was characterized by a gradual and painless increase in size over time. The patient reported no other swellings and indicated that there was no history of similar masses within her community. Moreover, she denied any previous trauma related to the area. There were no indications of chronic cough, excessive night sweats, radiation exposure, or significant fluctuations in her weight. She did not display intolerance to temperature extremes and did not experience excessive sweating. There was no record of tremors or anxiety. While the patient noted a slight alteration in her voice, she did not report any difficulties with breathing or swallowing. Additionally, there were no observable exophthalmos or visual impairments. She had a known history of hypertension for over 15 years, which was managed through medication. The patient was allergic to chloroquine (an antimalarial agent), and had discontinued her use of vasoprin prior to surgery. Her surgical history included an appendectomy performed 16 years earlier. The individual is a widow with eight children; her last pregnancy occurred 28 years ago, and she has been postmenopausal for 26 years.

Clinical examination indicated that the patient appeared to be in no apparent distress; she was afebrile, exhibited no pallor, and showed no signs of pedal oedema or peripheral lymphadenopathy. A hard mass was palpated, affecting the isthmus and left lobe of the thyroid gland, measuring 12 x 6 cm at its widest points, accompanied by tracheal deviation to the right. The mass was mobile, shifting with swallowing and partly located in the anterior inferior region as shown in Figure **1**.

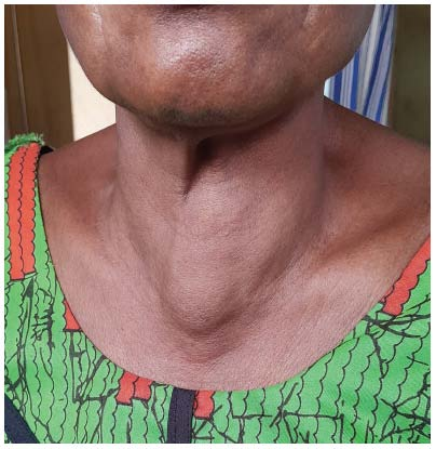


Figure 1: Clinical photograph of the nodular disease of the thyroid.

It was not adhered to the skin and was also mobile. There were no signs of cervical lymphadenopathy. Both chest and abdominal examinations yielded unremarkable results. A clinical diagnosis of a hard thyroid nodule was established.

The work-up included: Full blood count (FBC) - PCV 37% (35-55), white blood cell (WBC) - total 6.5 x 10^3/µl (4-12), neutrophils 18% (50-60), eosinophils 7% (0-5), basophils 0% (0-2), lymphocytes 75% (25-50), monocytes 0% (2-10). Thyroid function test (TFT) – T4 – 5.6 µg/dl (4.9-11.00), T3 – 1.27 ng/ml (0.79-1.58), TSH 2.0 µIU/ml (0.38-4.31). Serum calcitonin < 1.0 ng/l, Ca2+ 2.5 mmol/l (2.1-2.6), alkaline phosphatase 18 mmol/l (22-92). Urinalysis was normal. Chest X-ray - tracheal deviation to the right with features of hypertensive heart disease, X-ray of the neck (AP & lateral) – showed a retrosternal extension, Figure **2**.

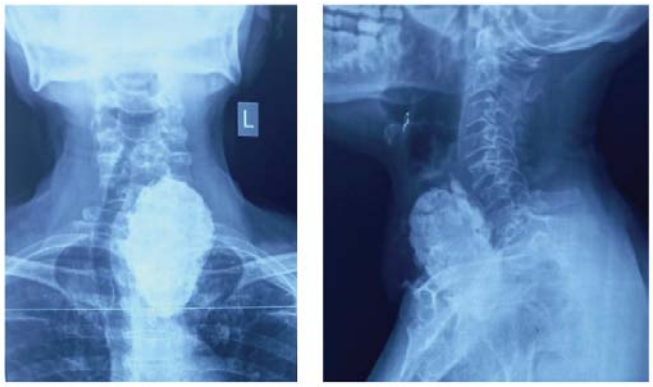


Figure 2: Neck X-ray that showed a calcified nodule with retrosternal extension and displacement of the trachea to right.

USS showed a normal right thyroid and lobulated calcified left thyroid lobe. Indirect laryngoscopy was reported as normal. Fine needle aspiration biopsy(FNAB) was not done as the nodule was stonily hard at clinical evaluation.

She was offered partial thyroidectomy (isthmustectomy and left lobectomy) in February 2025, Figure **3**.

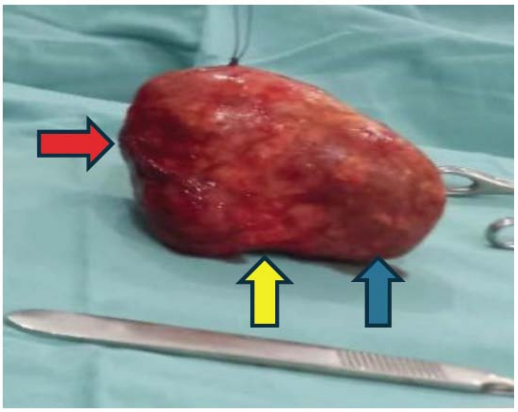


Figure 3: Thyroidectomy specimen: Red-arrow-anterosternal part, yellow arrow- part overriding the sternum and blue arrow- retrosternal portion.

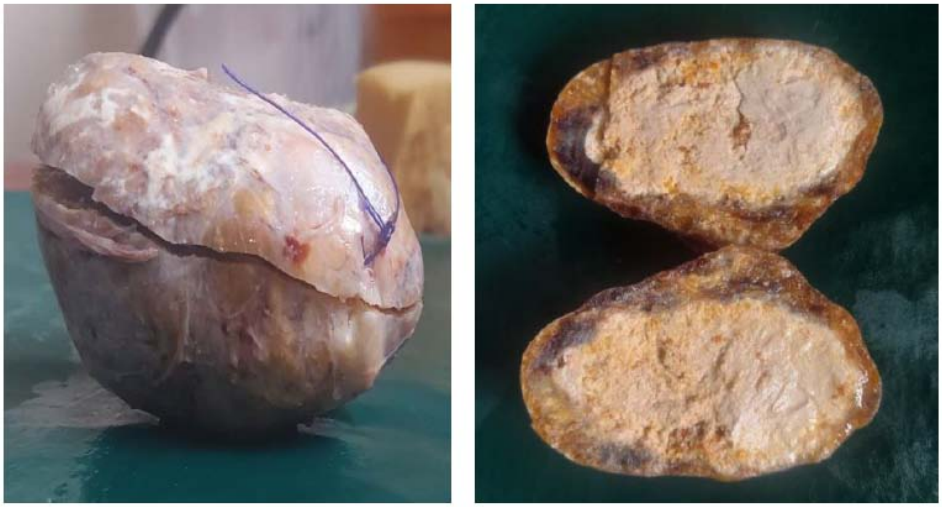
The findings at surgery were: 1. Atrophic strap muscles with the thyroid capsule morbidly adherent to the gland. 2. The left lobe of the thyroid and the isthmus were rocky hard. 3. A diamond/triangular-shaped nodule with the anterior inferior anterosternal pole overlying the sternum and the posterior inferior pole plunging retrosternal. The resected thyroid nodule was submitted for histology, Figure **3**. Estimated blood loss was approximately 300 ml. The postoperative period was satisfactory, and the patient was discharged to the outpatient department. During a subsequent visit, she presented with the histology report. Gross - the thyroid nodule weighed 250 g and measured 10 x 7.5 x 4.5 cm. It was solid and stony hard, Figure **4a**. The cut section showed a chalky, gritty surface with compressed thyroid tissue in the periphery, Figure **4b**.

Microscopy sections showed compressed thyroid with variable-sized follicles filled with pale colloidal material lined by cuboidal to flattened epithelial cells. It overlaid a calcified core, with no atypia, Figure **5**. The definitive diagnosis was TN - colloid goitre with calcific degeneration.

Follow-up was satisfactory without postoperative complications. The postoperative thyroid function test was normal six months after surgeryin August 2025.The patient's symptoms and anxieties were fully resolved, resulting in a return to normative quality of life(QOL).

DISCUSSION

Thyroid nodules are a common endocrine condition, and the detection rate is up to 68% in adults [10,12]. A giant TN is defined as a nodule larger than 4 cm [13]. Most TNs are benign. Despite the high prevalence of thyroid nodular disease, 7-15% of the nodules are malignant, depending on various factors associated with the patients [1,5]. The frequency is higher in women and the elderly, in keeping with our experience [1]. In an iodine-sufficient environment, the prevalence of palpable TNs is higher in women than in men,



a **b**

Figure 4: a) Gross revealed a nodule that weighed 250g and measured 10 x 7.5 x 4.5cm, solid and stony hard. **b**) Cut section showed chalky, gritty surface with compressed thyroid tissue in the periphery.

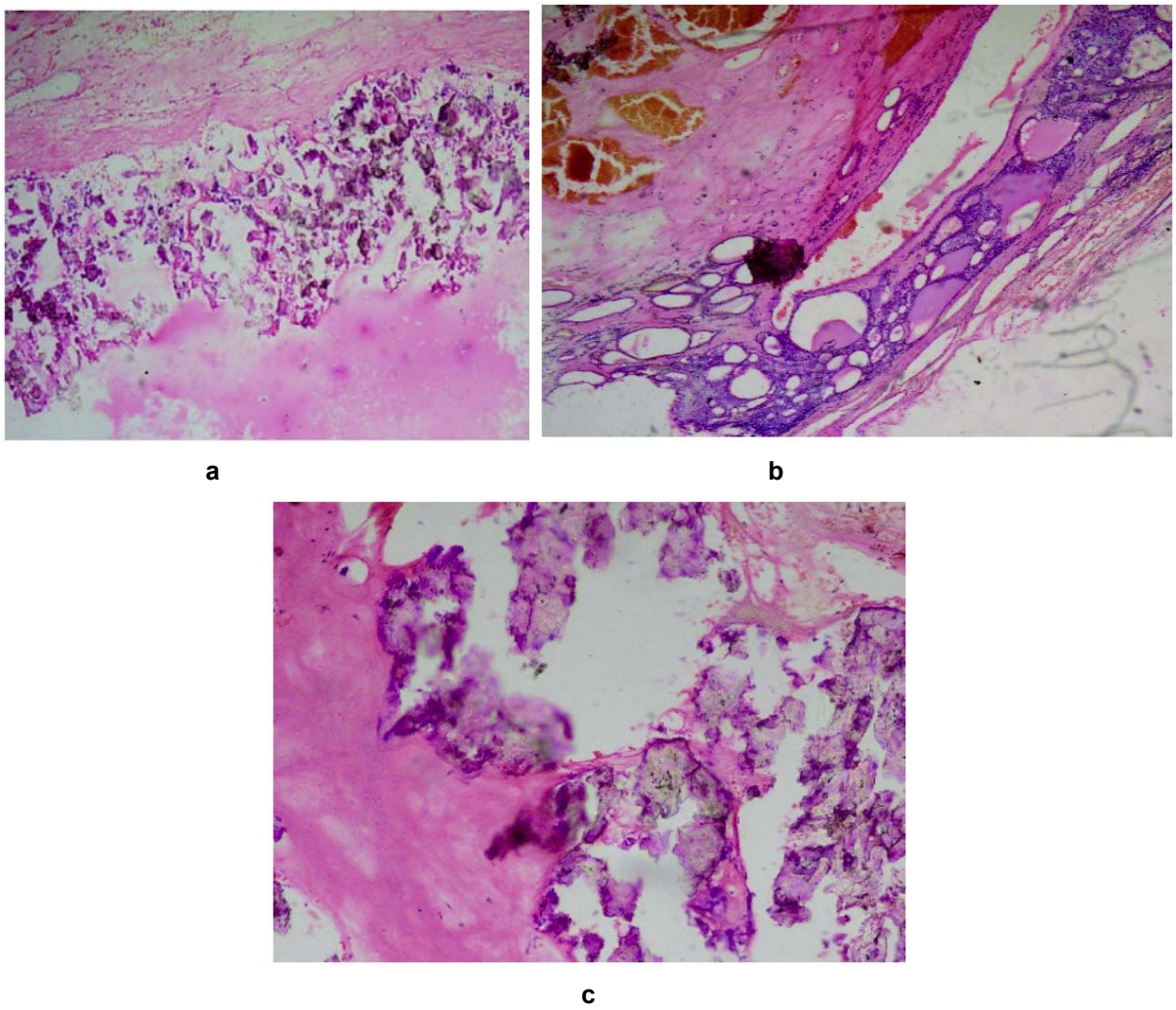


Figure 5: a) H&E x 100- Section showing extensive calcification with atrophic thyroid follicles and a surrounding fibrous intact capsule. **b**) H&E x 100- Section showed compressed thyroid with variable-sized follicles filled with pale colloidal material lined by cuboidal to flattened epithelial cells. It overlaid a calcified core, with no atypia, **c**) H&E x 400- Section showing extensive calcification with a pool of colloid - The definitive diagnosis was TN - colloid goitre with calcific degeneration.

approximately 5% in women and 1% in men. The lifetime risk of developing a palpable TN increases with age, estimated at 5-10% [5,6].

Haemorrhage, epithelial degeneration, or tissue necrosis predispose individuals to dystrophic calcification in a goitre of long duration [9,14]. Ionizing radiation, increased or decreased dietary iodine effect, family history of thyroid cancer, and hereditary syndromes are risk factors for thyroid cancer [1]. The intraglandular localization of a nodule has been shown to be an independent risk factor for malignancy: nodules located in the isthmus demonstrate the highest risk of cancer diagnosis. The lowest risk is associated with the lower third of the lobe when compared with the middle and upper poles [15]. The risk of malignancy is three times higher in females than in males; however, the risk of malignancy is higher in male patients with TN [16]. Many benign and malignant diseases present as TNs [1]. Thyroid-stimulating hormone is the main mitotic factor responsible for the high incidence of TNs in endemic goitre regions associated with iodine deficiency [17].

The majority of TNs are benign and pose minimal risk [18]. Malignant TNs, although rare, can become a psychological burden to patients due to potential metastasis, particularly in high-risk patients. Accordingly, it becomes crucial to differentiate between benign and malignant TNs [19]. Calcification may be present in both benign and malignant TNs, and it is not a specific marker [19,20]. However, the assessment of the pattern of calcification can be utilized to differentiate between benign and malignant nodules [8]. Calcifications are categorized into three types: microcalcification, macrocalcification, and peripheral calcification. A higher risk of malignancy is associated

with microcalcifications [19]. Thyroid calcifications are divided into two types: microcalcification based on dimensions and echogenic characteristics of less than 2 mm in diameter, and macrocalcification greater than 2 mm with a posterior acoustic shadow [8]; some reports state 1 mm or less [20]. Microcalcification is associated with PTC and is found in up to 40% of cases. Regarding macrocalcification TNs, peripheral rim or egg-shell calcification has been associated with multinodular goitre (MNG) and is generally considered an indicator of a benign nodule [20]. Peripheral calcification is the most commonly seen pattern in MNG. Some studies have suggested an increased rate of malignancy in nodules with peripheral calcification [10].

The clinical evaluation of TNs detected is centred on the risk of cancer, presence of hyperfunction, and symptoms and signs of compression [12,21]. Clinical evaluation cannot determine the composition and nature of the TN. However, some clinical features may raise suspicion of malignancy. The history of head and neck radiation should be sought, including the history of familial thyroid cancer [1]. As part of the assessment, age and gender should be considered. Ages at detection younger than 14 years and older than 70 years are associated with a higher risk of malignancy [1]. The patient may be asymptomatic, exhibiting no symptoms of compression, hyperthyroidism, or hypothyroidism, as was the experience with our patient. Symptoms may develop based on the size, composition, and function of the nodule. Calcified nodules tend to grow slowly over a long duration. The differential diagnosis of anterior neck swelling includes cystic lesions in the midline, thyroglossal cyst, and dermoid cyst, which may also become calcified. Laterally, a branchial cyst may be found. Lipomas, which may also be calcified, should be considered a differential. Rarely, the lesion may be a lymph node or lymphoma. Benign or malignant nodular growth may arise from the connective or supporting tissue surrounding the thyroid follicle [3]. We presented a 68-year-old woman with a rare case of a massive calcified benign nodular disease of the thyroid that involved the isthmus and the left lobe in the anterosternal, retrosternal, and retro-clavicular locations with the deviation of the trachea to the right. The anterosternal part of the nodule was adherent to the atrophic strap muscles, with the thyroid capsule morbidly attached to the nodule due to pressure. In the anterior relation of the neck, the strong and thick investing layer of the deep cervical fascia, along with the strap muscles, prevents the forward enlargement of the thyroid. Consequently, the thyroid is normally directed into the superior mediastinum [4]. In our case, the anterior support was anatomically weak from pressure caused by the calcified nodule, hence the anterosternal extension of the TN pushing through the weakanterior layer as confirmed during surgery. In depth, the TN displaced the trachea to the right but without compression, as shown on the X-ray of the neck. Bianchi *et al*. described a case of multinodular goitrein a 76-year-old woman with multinodular goitre that showed a mixed pattern of calcification (microscopic and macroscopic) without symptoms of obstructionin keeping with our study [8]. Also similar to our report, Goyal *et al*. reported a 52-year-old woman with a calcified left-sided neck swelling of six years' duration with trachea deviation without compressive symptoms [24]. Kim *et al*. reported that annular calcification was associated with the lowest risk of malignancy [25]. Jayarajah *et al*. reporteda large calcified nodule ina70-year-old man with goitre of 30 years duration associated with difficulty in breathing with intermittent dysphagia for solids [9]. Lyons *et al*. described a large retrosternal calcified goitre in an 82-year-old man with calcified goitre with obstructive symptoms and tracheal deviation. Symptoms may, in addition to calcified nodules, present with calcifications in the surgical tissue plane [26].

The major laboratory investigations are serum thyroid stimulating hormone (TSH), which provides information about the function of the gland. Thyroglobulin (Tg) is frequently used as a biomarker in monitoring recurrence in patients after thyroidectomy for follicular-derived thyroid cancer. Calcitonin is a biomarker used in the diagnosis as well as follow-up of parafollicular C-cell derived medullary thyroid cancer (MTC) [1,2]. Imaging with neck X-ray may be utilized in determining the extent of the goitre, including calcification and the position/compression of the trachea [9]. High-resolution USS is the current standard for the initial evaluation of TNs. In USS, the presence of microcalcification is generally accepted as the most reliable indicator of malignancy, with a specificity of 85-94% and a positive predictive value (PPV) of 69-71%7. However, due to overlapping features between benign and malignant lesions, the diagnostic precision may be limited [1,10]. The Ultrasonography Risk Classification is based on the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS)1. The CT and MRI are not in routine use in the initial evaluation of TNs and have no reliable findings that differentiate benign and malignant TNs [1]. However,

CT is required for the evaluation of retrosternal TNs in patients that present with symptoms of compression of the trachea, oesophagus, and vessels in the superior mediastinum [5].

FNAB is the gold standard for the evaluation of TNs [3]. It can be performed in the outpatient setting. It is a fast and safe method with high sensitivity, specificity, precision, and accuracy in differentiating between benign and malignant nodules [27]. There is a challenge in performing FNAB on completely calcified nodules [8]. This was the experience with our patient. Accordingly, this necessitates thyroidectomy without biopsy based on clinical evaluation of the patient in view of the low probability of obtaining a good sample for diagnosis [7]. In some cases, questionable cytology may necessitate surgery [28]. A definitive diagnosis from histopathology can be made after a complete nodule or thyroid gland specimen is evaluated [29].

The diagnosis and treatment of TNs are controversial. The major indications for surgery in TNs include the presence of malignancy, hyperfunction, and compression symptoms of a nodule [1,12]. When surgery is indicated, the extent of the resection (lobectomy or total or near-total thyroidectomy) will depend on many factors, including the diagnosis of the disease, symptoms, presence of a nodule in the contralateral lobe, functional status of the thyroid, comorbidities, surgical risk, and patient preference [1] . Our patient had left lobectomy and isthmustectomy as the contralateral lobe was normal in the setting of benign disease.Surgical intervention for calcified giant nodular disease of the thyroid presents distinct technical challenges due to the large, hard nature of the mass and potential anatomical distortion. These challenges significantly increase the risk of complications such as recurrent laryngeal nerve (RLN) injury and massive haemorrhage [26]. Dissection difficulties arise from compression, displacement and adhesions of surrounding vital structures (trachea, oesophagus, and major blood vessels), rendering normal anatomical landmarks unreliable. Calcification makes the gland immobile and fixed to adjoining tissues. The mass is hard to manipulate and dissect [24]. Long-standing giant nodules develop severe fibrosis and adhesions to adjacent structures, especially the trachea and prevertebral fascia [9]. The size limits the surgical field of vision. The risk of RLN injury arises due to nerve displacement/compression, traction injury, and obscured visualisation [9]. Surgeonsmanaging these cases face critical decisions at multiple points: extent of surgery, surgical approach, nerve monitoring, and parathyroid gland preservation. Effective management relies on the experience of the surgical team, comprehensive preoperative imaging (CT), and a meticulous surgical technique to navigate the challenges safely [8]. The prognosis following appropriate management (surgery if symptomatic or observation of tracheal deviation in asymptomatic) is very favourable with a high likelihood of symptoms resolution and no cancer related concerns [9].

In conclusion, extensive calcification in nodular diseases of the thyroid is a rare clinical manifestation that may present significant diagnostic difficulty. The adhesion of enlarged nodules to surrounding tissues highlights considerable challenges in surgical intervention. Imaging techniques are crucial for effective surgical planning, while histological examination is considered the definitive method for diagnosis. It is advisable to pursue early intervention in conjunction with a collaborative multidisciplinary approach.

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ETHICAL APPROVAL

The requirement for ethical approval was waived as this study constitutes a case report on a patient treated by our team, rather than an interventional study; thus, no interventions or experimental procedures were conducted on the patient for the purposes of this research.

INFORMED CONSENT

The patient provided both verbal and written informed consent for the documentation of this case and the associated images.

CONFLICT OF INTEREST DECLARATION

The authors declare that there are no potential conflicts of interest concerning the research, authorship, or publication of this article.

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DATA AVAILABILITY STATEMENT

Data supporting the findings of this paper are available and can be accessed upon request.

AUTHOR CONTRIBUTIONS

Dr Nwagbara was responsible for conceptualizing and drafting the manuscript. Dr Ashindoitiang contributed to the manuscript writing and served as the corresponding author. Dr Ugbem provided histological diagnosis and assisted in the manuscript writing. Dr Matthias was involved in histological diagnosis, while Dr Obeten contributed to the collection of materials. Prof. Asuquo oversaw the project and participated in writing the manuscript.

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