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A Rare Case Report: Non-Fusion of Thyroid Medial and Lateral Anlage with Presence of Substernal Anterior Mediastinal Extension Presenting As Multinodular Goiter

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Abstract

The thyroid gland develops through the fusion of the medial thyroid anlage, originating from the primitive pharynx, and the lateral thyroid anlage, derived from the ultimo branchial structures. Proper fusion of these components is essential for normal thyroid development and function. However, in rare cases, incomplete or failed fusion can lead to congenital anomalies, such as non-fusion of the medial and lateral anlagen or complete non-fusion of all thyroid lobes. Non-fusion of the medial and lateral thyroid anlagen can result in anatomical variations, including the absence of the tubercle of Zuckerkandl, incomplete thyroid lobe formation, or altered perifollicular C-cell distribution. Clinically, this anomaly may present as thyroid asymmetry, ectopic thyroid tissue, or an increased risk of nodular thyroid disease. An even rarer anomaly is the complete non-fusion of all thyroid lobes, which may lead to the development of ectopic lobes, solitary lobe formation, or an absent isthmus, all of which can have implications for thyroid hormone synthesis and surgical management. This paper reviews the embryological basis of these rare anomalies, examines documented cases, and discusses their clinical significance in thyroid pathology and surgical planning. Awareness of these variations is crucial for surgeons, radiologists, endocrinologists, and pathologists to prevent misdiagnosis and optimize patient care. Here, we present a case of a middle- aged female with complete non-fusion of all thyroid lobes, accompanied by a retrosternal goiter that was distinct from the primary thyromegaly. Histopathological examination confirmed the diagnosis of colloid multinodular goiter in a thyroid state.

Keywords: Total thyroidectomy, Multinodular goiter, Non-fusion of medial and lateral thyroid anlage, Congenital anomaly and aberrant anatomy, retrosternal goiter.

Introduction

A thorough understanding of thyroid embryology is essential for head and neck and general surgeons, as congenital anomalies can significantly impact surgical outcomes. The thyroid gland, the first endocrine organ to develop, originates from the endoderm of the primitive pharyngeal floor at the foramen cecum around the 24th day of gestation (Arrangoiz et al., 2018).The thyroid primordium descends anterior to the hyoid bone and laryngeal cartilages, remaining connected to the tongue via the thyroglossal duct, which typically regresses by the seventh week (Patel & Bhatt, 2019).

In approximately 50% of individuals, the distal thyroglossal duct persists; forming a pyramidal lobe, sometimes attached to the hyoid bone via the levator glandular thyroidal (Rajkonwar & Kusre, 2016). Fusion of the median thyroid anlage with the ultimo branchial bodies facilitates the incorporation of perifollicular (C) cells, which are localized along the central lobar axis and derived from neural crest precursors. Thyroid follicular cells, evident by the eighth week, begin colloid production and radioactive iodine uptake by the 11th week, marking the onset of thyroxine synthesis (Arrangoiz et al., 2018).

Congenital thyroid anomalies arise from disruptions in development, migration, or differentiation (De Felice & Di Lauro, 2004).Thyroglossal duct cysts result from incomplete duct obliteration, while ectopic thyroid tissue, most commonly lingual thyroid, arises from failed descent. Thyroid hemi agenesis, agenesis, and hypoplasia can lead to congenital hypothyroidism, whereas pyramidal lobe persistence is a common anatomical variant (Szczepanek-Parulska et al., 2017).

We report a novel case of a middle-aged female with complete non-fusion of all thyroid lobes during total thyroidectomy

for a massive multinodular goiter, accompanied by a distinct retrosternal goiter. Histopathological examination confirmed colloid multinodular goiter in a thyroid state. This represents the first documented case of total thyroid lobe non-fusion worldwide. Awareness of such rare anomalies is critical for accurate diagnosis, surgical planning, and optimizing patient outcomes.

Case Report

A 63-year-old female presented to our outpatient department with a history of swelling in front of the neck for the past 10 years. The swelling had an insidious onset and gradually increased in size over the first nine years. However, the patient noted a consistent and more rapid increase in size over the past year, prompting her to seek medical attention. Over the last six months, she developed progressive dysphagia to solid foods, and in the last four months as well experienced orthopnea. Her past medical history revealed a diagnosis of reactive airway disease, for which she intermittently used inhalational steroids during acute exacerbations. Serial thyroid function tests had always been within normal limits, and she had never exhibited any symptoms suggestive of hyperthyroidism or hypothyroidism. Apart from her presenting complaints, she was in good overall health and was not on any regular medications.

Fig No.01 On physical examination, she had gross thyromegaly measuring 11 × 6 cm with multiple palpable nodules in both lobes, the largest being 4 × 3 cm on the left side. The nodules exhibited variable consistency, and the swelling moved with deglutition, but its lower margin was not appreciable. (Fig No.01) Percussion over the upper sternum revealed a dull note. The carotid arteries were displaced laterally, but there were no signs of venous congestion, cervical lymphadenopathy, or any other masses elsewhere in the body. Her general systemic examination was unremarkable.

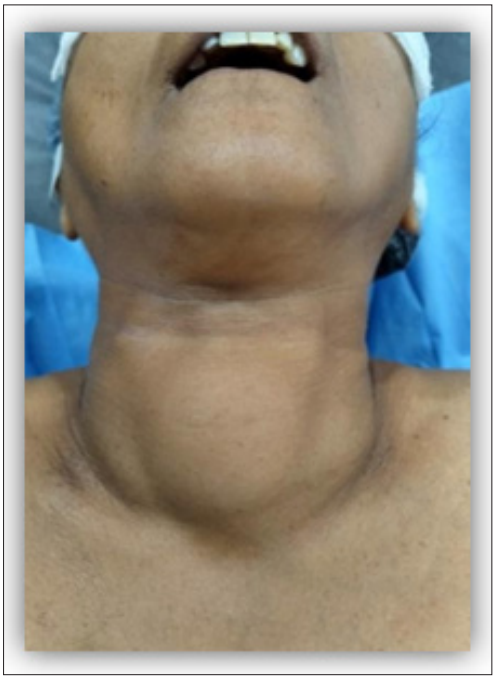


Figure 1: Image showing clinical presentation of thyroid multinodular goiter.

Given the complexity of the Multinodular goiter and possible retrosternal involvement, a contrast-enhanced CT scan was performed. The scan showed bilateral thyroid lobe enlargement with multiple nodules of varying sizes. Hypodense areas were noted in the left lobe and isthmus, while the rest of the gland displayed calcifications and hyperdense regions. The right lobe measured 3 × 3 cm, while the left lobe measured 4.3 × 5.1 cm, extending superiorly to the C4 vertebral level and inferiorly with retrosternal extension reaching the D3 level. (Fig No, 02, 03, 04) Posteriorly, the mass displaced the trachea to the right and anteriorly, while posteromedial, it was abutting the esophagus. (Fig No.05, 06) Post-contrast imaging revealed heterogeneous enhancement, with no evidence of cervical or mediastinal lymphadenopathy. The parathyroid glands appeared normal. A videolaryngoscopic examination confirmed normal, mobile vocal cords. (Fig No.07).

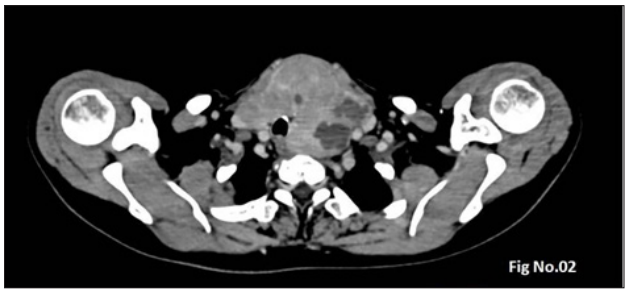


Figure 2: Axial images of CECT Neck demonstrating multinodular goiter with variable consistency. Hypo dense areas were noted in the left lobe and isthmus, while the rest of the gland displayed calcifications and hyper dense regions.

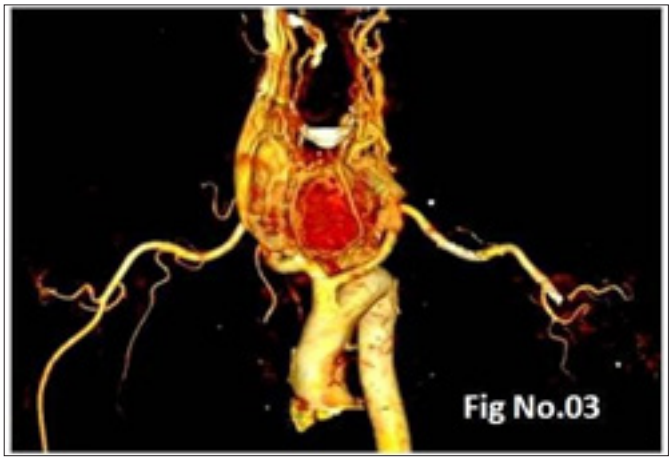


Figure 3: Image showing 3D reconstruction of the thyroid and the surrounding vasculature and vascularity within the thyroid gland.

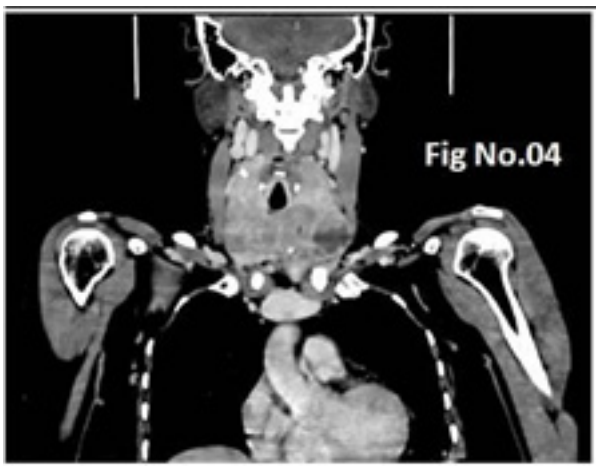


Figure 4: CECT Neck and thorax showing the thyroid lobes with extension superiorly to the C4 vertebral level and inferiorly with retrosternal extension reaching the D3 level.

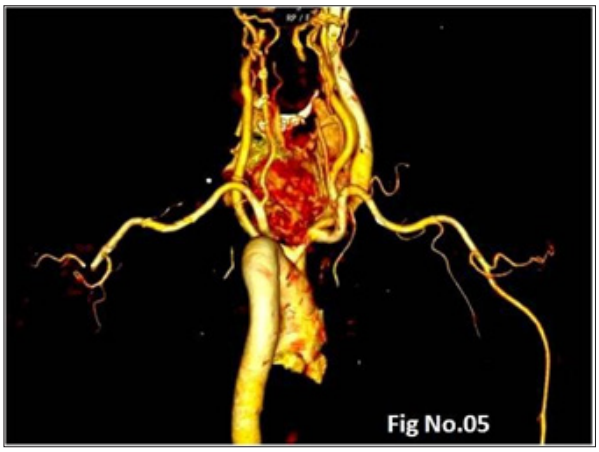


Figure 5: 3D Reconstruction of the CECT Neck and Thorax.

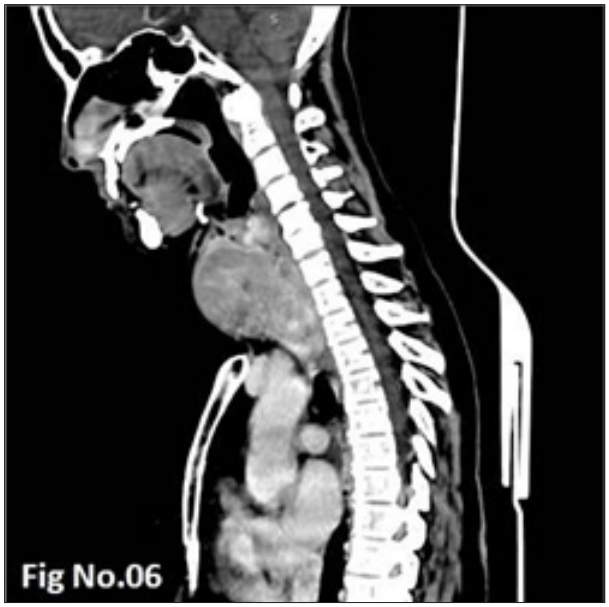


Figure 6: Sagittal cuts CECT – both images showing the retrosternal extension reaching the D3 level, posteriorly, the mass displaced the trachea to the right and anteriorly, while posteromedially, and it was abutting the esophagus.

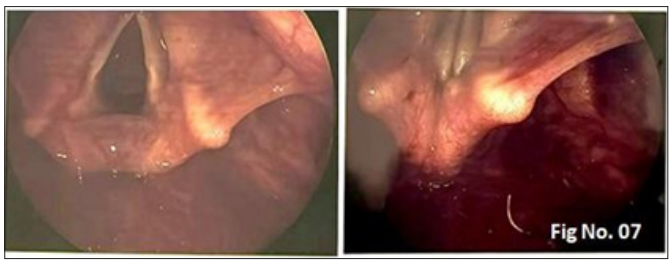


Figure 7: Showing normal mobile vocal cords on videolaryngoscopy.

Following comprehensive preoperative evaluation and informed consent, the patient underwent total thyroidectomy. Intraoperatively, the right lobe, isthmus, and left lobe were found to be separate entities and non-fused, each with an independent blood supply. The retrosternal thyroid tissue was distinct from the main thyromegaly and was positioned over the brachiocephalic and left common carotid arteries. (Fig No.08, 09, 10) A cervical approach was used to meticulously dissect and excise the retrosternal goiter while ensuring hemostasis. All four parathyroid glands, along with the bilateral recurrent and superior laryngeal nerves, were carefully preserved. The patient had an uneventful immediate postoperative recovery.

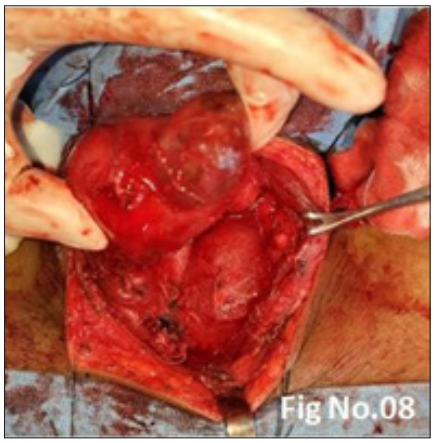


Figure 8: Image depicting intraoperative dissection of right lobe of thyroid with separate left lobe lying beneath

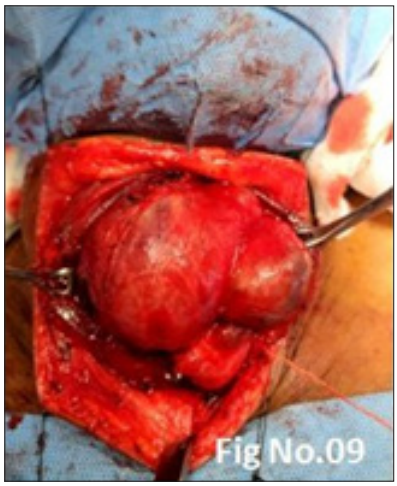


Figure 9: Intra operative Image showing delivering of right lobe into to securing the vascularity and preserving the vital structures

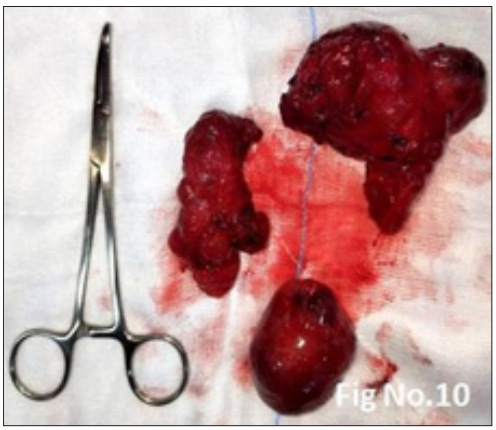
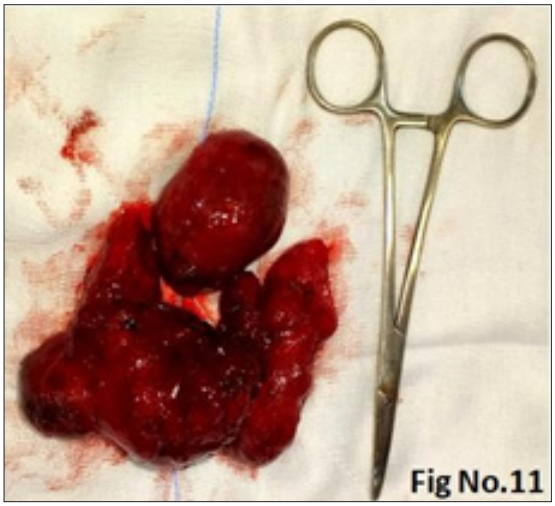


Figure 10: Image showing individual isolated lobes of thyroid and the retrosternal goiter.

Postoperatively, the patient was started on levothyroxine and vitamin D3 supplementation. She has been on regular follow-up, and her histopathological report confirmed a simple colloid multi-nodular goiter. (Fig No.11, 12, 13, 14) The patient continues to do well, with no postoperative complications or recurrence of symptoms.



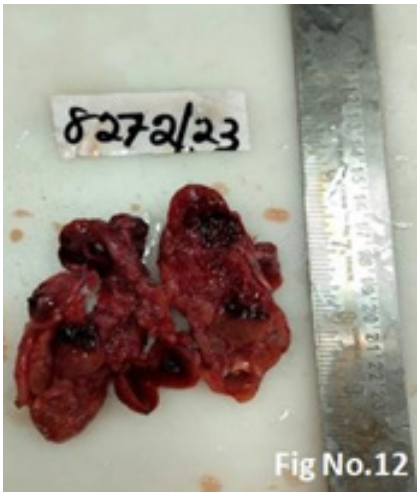


Figure 11&12: Image showing gross appearance of the specimen sent to the pathology lab - Multinodular goiters are asymmetric, Nodular and bumpy outer surface and variegated cut surface, cystic and hemorrhagic with brown gelatinous colloid nodules with focal calcification.

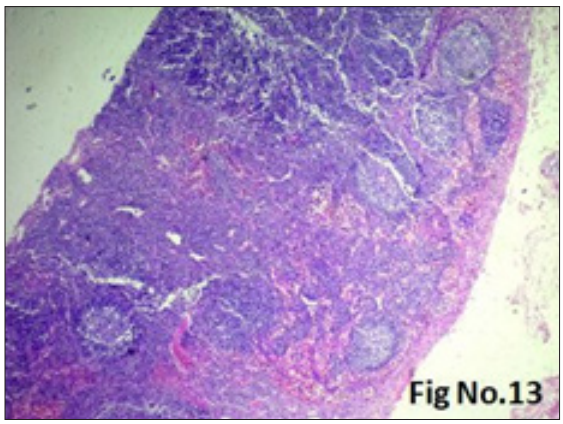


Figure 13: HPE showing Nodules with variable histological patterns: from colloid and microfollicular to hypercellular / microfollicular.

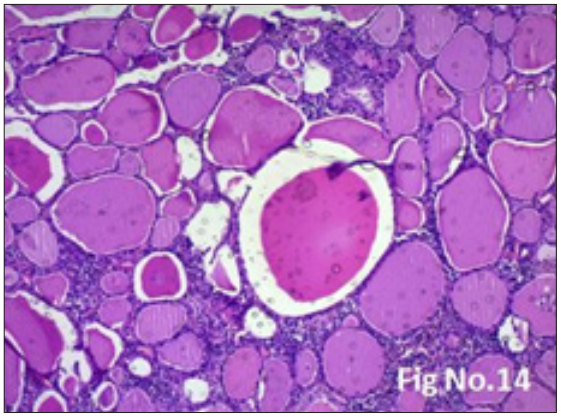


Figure 14: Secondary changes may be seen, including foci of fresh or old hemorrhage, rupture of follicles with granulomatous response, fibrosis, calcification and even osseous metaplasia. Some of the cystically dilated follicles may show papillary projections (Sanderson polsters) that may mimic papillary carcinoma; however, they lack the nuclear features of papillary carcinoma.

Discussion

A modern surgeon must possess a thorough understanding of thyroid embryogenesis and its congenital anomalies, as these factors influence surgical outcomes and complications. The thyroid gland, the first endocrine organ to develop, originates as an endodermal outpouching of the primitive foregut around the 24th day of gestation. It arises from the median pharyngeal floor between the first and second branchial pouches at the foramen cecum, with a dual embryologic origin from the primitive pharynx and neural crest (Arrangoiz et al., 2018).

The thyroid primordium initially forms as a midline thickening, which develops into the thyroid diverticulum (anlage). This structure solidifies to form the follicular elements; eventually dividing into two lateral lobes connected by an isthmus (Assi, 2023).The descending thyroglossal duct loses its lumen by the fifth week and regresses, leaving the foramen cecum as its remnant. By the seventh week, the thyroid reaches its final position.

Lateral thyroid anlages, derived from the fourth and fifth branchial pouches, fuse with the median thyroid anlage around the fifth week, contributing up to 30% of the gland's mass (Boyd, 1950). These neuroectodermal- derived anlages give rise to calcitonin-producing perifollicular (C) cells, which migrate from the neural crest to the ultimo branchial bodies and localize in the superior posterior thyroid lobes. Fusion occurs at the tubercle of Zuckerkandl, restricting C cells to the middle and upper thirds of the lateral lobes (Irawati et al., 2016).

Thyroid follicular cells, derived from the median thyroid anlage, emerge by the eighth week, with colloid production initiating by the 11th week, marking thyroxine synthesis onset. Follicular development follows three stages: pre-colloid (7–13 weeks), colloid (13–14 weeks), and follicular (beyond 14 weeks), with follicle formation via budding or division (Dom et al., 2021).

Thyroid morphogenesis relies on transcription factors TITF-1 (Nkx2), Foxe1 (TITF-2), and PAX-8. (Table No.01) Genetic mutations affecting these factors can result in abnormal migration or agenesis (De Felice & Di Lauro, 2004). Ongoing research aims to identify genes responsible for initial thyroid differentiation, potentially elucidating true thyroid agenesis mechanisms.

GENE	CHROMOSOME		FEATURE OF THE GENE PRODUCT
	MOUSE	HUMAN	
Titf1/Nkx2-1	12 C1-3	14q13	Homeodomain transcription factor
Pax8	2	2q12-14	Paired domain transcription factor
Foxe1	4	9q22	Forkhead domain transcription factor
Hhex	19	10	Homeodomain transcription factor
Tshr	12	14q31	G protein coupled receptor
Nkx2-5	17	5q34	Homeodomain transcription factor
Fgfr2	7	10q26	Tyrosine kinase receptor
NIS	8	19p13	NIS; membrane protein with 13 putative transmembrane domains

Table 1: Genetics involved in the thyroid embryogenesis (De Felice & Di Lauro, 2004)

Ectopic thyroid tissue, resulting from migration anomalies, poses diagnostic challenges, particularly in the substernal or mediastinal regions, where it may mimic thymic masses, retrosternal goiter, or mediastinal malignancies. Multinodular goiter in non-fused thyroid tissue can exacerbate compressive symptoms, including vascular compression, dysphagia, and dyspnea.

Understanding these anomalies is crucial for surgical precision, ensuring complete thyroidectomy when necessary. Atypical thyroid anatomy may alter standard surgical landmarks, necessitating preoperative imaging and intraoperative caution (Germano et al., 2014). Cross-sectional imaging, particularly contrast-enhanced CT, is essential for delineating gland extent and identifying ectopic tissue. The embryological basis of these anomalies suggests disruption in lateral and median anlage interactions during early fetal development, possibly due to genetic or environmental factors. A deeper understanding of these rare variations enhances surgical preparedness, reducing inadvertent tissue preservation or structural damage (Lee et al., 2021).

This case underscores the need for greater awareness among surgeons and endocrine specialists regarding rare thyroid developmental abnormalities. Early identification and appropriate surgical planning are critical for optimal patient care. Further research and case reports are needed to clarify underlying embryological mechanisms and establish standardized surgical approaches for these uncommon presentations (Ludwig et al., 2023).

Conclusion

An experienced and perceptive general and endocrine surgeon must possess a thorough understanding of normal thyroid anatomy and its embryonic development. It is crucial for surgeons to recognize congenital aberrations during the perioperative period to prevent intraoperative and postoperative complications. Additionally, they should remain vigilant about the potential presence of an undetected ectopic thyroid, which may be malignant. Therefore, an in-depth knowledge of thyroid anatomy and its variations is essential to avoid overlooking such anomalies when managing thyroid disorders. A comprehensive literature review on this subject revealed no reported cases of thyroid lobe non-fusion occurring alongside a separate retrosternal goiter, with histopathological findings confirming simple colloid multinodular goiter. Surgical intervention remains the preferred treatment for retrosternal goiter, regardless of symptom presentation. In most cases, the goiter can be effectively removed through a single neck incision, a less invasive approach that promotes faster recovery. Further research on thyroid embryogenesis, anatomical anomalies, and their genetic correlations is necessary to facilitate comprehensive genetic mapping and optimize preoperative imaging strategies.

Author Contributions

Collection and/or Assembly of Data

Anand Bhandary Panambur, Paraashar R Rai.

Manuscript Writing and Approval

Anand Bhandary Panambur, Thoppil Reba Philipose.

Conflict of Interest Statement

The Authors Have No Conflicts Of Interest To Declare.

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