

Poorly differentiated thyroid carcinoma arising from substernal goiter: a case report

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- Malignant neoplasms arising from substernal goiter are extremely rare.
- Poorly differentiated thyroid carcinomas constitute approximately 2-4% of all thyroid neoplasms.
- Turin Criteria highlights the challenges in the diagnosis of poorly differentiated thyroid carcinoma.
- Computed tomography is fundamental in substernal goiter for surgical interventions evaluation and assessment of the substernal components.

Abstract

Introduction and importance:

Poorly differentiated thyroid carcinomas represent a rare heterogeneous group of malignant tumors that constitute approximately 2-4% of all thyroid neoplasms. Substernal Goiter is defined as an enlargement of the thyroid gland that is located below the thoracic inlet. Malignant neoplasms arising from a substernal goiter were reported in only 2-3% of cases.

This case report has been reported in line with the SCARE Criteria.

Case presentation:

This article presents a 54-year-old Syrian female who presented at our institution due to dysphagia, dyspnea, cervical swelling, and loss of appetite. Following clinical and radiological examinations, total thyroidectomy with lymph node dissection was performed. Microscopic examination revealed an infiltrative growth pattern of insular, trabecular, and solid formations of epithelial cells with scant eosinophilic cytoplasm, hyperchromatic nuclei, and bizarre mitotic figures with areas of necrosis. Subsequently, the final diagnosis was

confirmed as a multifocal poorly differentiated thyroid carcinoma arising from a substernal goiter.

Clinical discussion:

The heterogeneity of histologic features of poorly differentiated thyroid carcinoma represents a diagnostic challenge. Diagnosis of poorly differentiated thyroid carcinomas is based on the Turin Criteria which highlights histopathological features. Computed tomography plays a major role in substernal goiter for further evaluation.

Conclusion:

In this manuscript, we aimed to present a unique case report with challenging diagnostic features including the rapid development of an infiltrative poorly differentiated thyroid carcinoma from a substernal goiter highlighting the importance of a detailed histopathological examination of thyroid nodules in the absence of significant medical history.

Keywords: Poorly Differentiated Thyroid Carcinoma; Substernal Goiter; Thyroid Nodules; Histopathological Examination; Case Report.

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Introduction

Poorly differentiated thyroid carcinomas (PDTC) represent a heterogeneous group of malignant tumors that constitute approximately 2-4% of all thyroid neoplasms. These tumors were first defined by Sakamoto et al and Carcangiu et al in 1983/1984 as tumors with an intermediate aggressiveness between well-differentiated thyroid carcinomas (DTC) and anaplastic thyroid carcinomas (ATC), although Granner et al described PDTC cases with no clear definition earlier in 1963. PDTC was officially categorized as a separate entity by the World Health Organization Classification (WHO) in 2004 [1,2]. Diagnosis of PDTC is based on the Turin Criteria which includes the absence of nuclear characteristics of papillary carcinoma, the presence of solid/insular/trabecular growth pattern in addition to at least one feature of the following: mitotic rate $>3/10$ HPFs, convoluted nuclei, and tumor necrosis [3].

Substernal Goiter SG is defined as an enlargement of the thyroid gland that is located below the thoracic inlet and mostly presents with compressive symptoms including dyspnea and dysphagia. SG usually affects patients in their fifth decade with a female predominance. Malignant neoplasms arising from a substernal goiter were reported in 2-3% of cases [4].

Herein, we present an extremely rare case of a poorly-differentiated thyroid carcinoma arising from a substernal goiter with challenging features to a patient who was admitted to Tishreen University Hospital.

Case Presentation

A 54-year-old Syrian female non-smoker and non-alcoholic presented at our institution with complaints of severe dyspnea, mild dysphagia, cervical swelling, and loss of weight and appetite for two months. Medical and family histories were unremarkable, and no history of exposure to ionizing radiation was mentioned.

On presentation, physical examination revealed a palpable painless hard-in-consistency mass in the inferior part of the neck. Oxygen saturation was 88% in room air and respiratory rate was 24 breaths per minute. Other signs including body temperature, pulse rate, blood pressure, and full-body examination were normal. Laboratory examination revealed mild anemia with no other abnormalities.

Computerized Tomography (CT) scan demonstrated a massive enlargement of the thyroid gland extending into the upper chest at the level of the aortic arch, narrowing the trachea and compressing the esophagus (Fig. 1).

Due to the compression symptoms, total thyroidectomy with lymph node dissection through sternumectomy was performed.

The macroscopic examination revealed an enlarged thyroid gland weighing 350g. The right lobe measured 5×4×4 cm, and the left lobe measured 13×8×7 cm, the cut sections of both lobes demonstrated ill-defined nodules of yellow-tan coloration with foci of central necrosis (Fig. 2).

Detailed morphological examination revealed an infiltrative growth pattern of insular, trabecular, and solid formations of neoplastic epithelial cells with scant eosinophilic cytoplasm, hyperchromatic convoluted nuclei, and bizarre mitotic figures (mitotic rate of approximately 20%) with areas of necrosis and hemorrhage (Fig. 3).

Histopathological examination of the rest of the tissue of the enlarged thyroid gland revealed variable-sized follicles full of colloid and lined by a single layer of normal cuboidal cells, and the surrounding stroma was infiltrated by inflammatory cells. Subsequently, the final diagnosis was confirmed as a multifocal poorly differentiated thyroid carcinoma arising from a substernal goiter with capsular and vascular invasion as well as positive margins (Stage T4M0N0). Although immunohistochemistry was not available at our institution due to lack of resources, diagnosis was confirmed through detailed morphological examination by two pathologists. After surgical resection, the patient was put on adjuvant radiotherapy of 60 Gy in two fractions. Unfortunately, the patient died one year later due to the development of pulmonary metastases.

Discussion

Although the diagnosis and classification of poorly differentiated thyroid carcinoma demonstrated revolutionized progress in the last few decades. The rarity of this neoplasm and the heterogeneity of histologic features highlight a major diagnostic challenge. PDTC constitutes approximately 4% of all thyroid neoplasms and mainly affects females in their fifth age similar to our case [5,6].

PDTC is associated with local invasion and regional lymph node metastases in approximately 50-85% of cases. Nevertheless, in our case, the neoplasm was restricted to the thyroid gland with no lymph node metastases. Male gender, older ages, extrathyroidal invasion, high mitotic rate, and distant metastases are associated with worse prognoses in PDTC [7,8].

Although these factors were not detected in our case, the major challenge was establishing an accurate histopathological diagnosis. PDTC mostly arises from follicular or thyroid carcinomas, whereas arising from a substernal goiter represents an exceedingly rare and challenging entity.

Substernal goiter SSG was first defined by Haller in 1749 as an enlargement of the thyroid gland extending into the mediastinum [9]. Later Katlic et al proposed that the retrosternal component must be more than 50% of the thyroid gland to establish the diagnosis [10].

In a study by Arici C et al, 12% of substernal goiter cases included malignant components. Another study by Nakaya et al in 2017 demonstrated malignancy in 11.3% of substernal goiter cases [11,12].

Radiological techniques play a major role in diagnosis and management. Although ultrasound has been considered the main imaging modality for thyroid diseases including nodular goiter, computed tomography is highly preferable in substernal goiter as in our case for surgical interventions evaluation and assessment of the substernal component [13,14].

Assessment of the solid/trabecular/insular (STI) component represents a controversial point that could affect the diagnosis and prognosis of PDTC. Despite the absence of definite criteria, several studies concluded that the extent of the STI component must be higher than 50% of the tissue, whereas focal and minimal infiltration excludes the diagnosis of a PDTC [8,15]. In our case, the STI component was predominant representing approximately more than 70% of the resected mass.

Histopathological examination of Hematoxylin-and-eosin sections plays the most critical role in the diagnosis of PDTC, whereas immunohistochemistry seems to play a minor role in the classification of this neoplasm [8]. In our case, morphological examination revealed an infiltrative growth pattern of insular, trabecular, solid formations of neoplastic epithelial cells with scant eosinophilic cytoplasm, hyperchromatic nuclei, and bizarre mitotic figures with areas of necrosis and hemorrhage. The absence of papillae as well as the nuclear features of papillary carcinoma (ground-glass nuclei) and medullary carcinoma (salt-and-pepper chromatin) excluded the diagnosis of the aforementioned neoplasms.

In addition to the aforementioned morphological characteristics, our case demonstrated unique and challenging diagnostic features. First, the multifocal growth pattern of neoplastic cells in both the right and left lobes demonstrates a more aggressive course of the rapidly-

proliferating neoplasm. Second, the histopathological examination of the rest of the tissue of the enlarged thyroid gland (350g) revealed variable-sized follicles full of colloid and lined by a single layer of normal cuboidal cells, and the surrounding stroma was infiltrated by inflammatory cells. Subsequently, the final diagnosis was confirmed as a multifocal poorly differentiated thyroid carcinoma arising from a substernal goiter, which adds a significant educational value by highlighting the importance of a detailed histopathological examination of nodular goiter.

TERT promoter mutations as well as *RAS* and *BRAF* point mutations are considered the most common genetic alterations in PDTC and are associated with a worse prognosis and an increased rate of distant and regional lymph nodes metastases, respectively. A study by Landa et al revealed that *RAS* mutations were mostly detected in more progressive cases of PDTC with distant metastases and histologically fulfilling the Turin criteria, whereas *BRAF* mutations distinguished smaller cases of PDTC with nodal metastases that were diagnosed based on the presence of necrosis and high mitotic rate irrespective of growth pattern (MSKCC criteria) [16,17]. Also, other genetic alterations were detected in the more aggressive types of PDTC including *TP53*, *MED12*, *ATM*, *RBM10*, and *EIF1AX* mutations [18]. In our case, molecular studies were not available due to economic restrictions, and the diagnosis relied on a detailed histopathological examination with clinical and radiological correlations.

Regarding treatment modalities, total thyroidectomy followed by ^{131}I therapy is recommended for all cases of PDTC, whereas adjuvant radiotherapy is recommended after surgery for more aggressive diseases including stage T4 and stage T3 with distant metastases [19,20].

Conclusion

We aimed to present a unique case report that highlights challenging diagnostic features including the rapid development of an infiltrative PDTC from a substernal in addition to the multifocal growth pattern of neoplastic cells in both the right and left lobes, aiming to highlight the importance of a detailed histopathological examination of all thyroid nodules in the absence of a significant medical and radio-exposure history. Also, this case is considered rare as only 2-3% of substernal goiter turn to malignancies.

List of abbreviations

PDTC: Poorly Differentiated Thyroid Carcinoma

US: Ultrasonography

CT: Computed Tomography

H&E: Hematoxylin and Eosin

Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Conflicts of interest disclosure

The authors declares that they have no conflicts of interest.

Provenance and peer review

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Not applicable.

Registration of the study

Not applicable because it is a case report and dose not involve clinical studies on human subjects.

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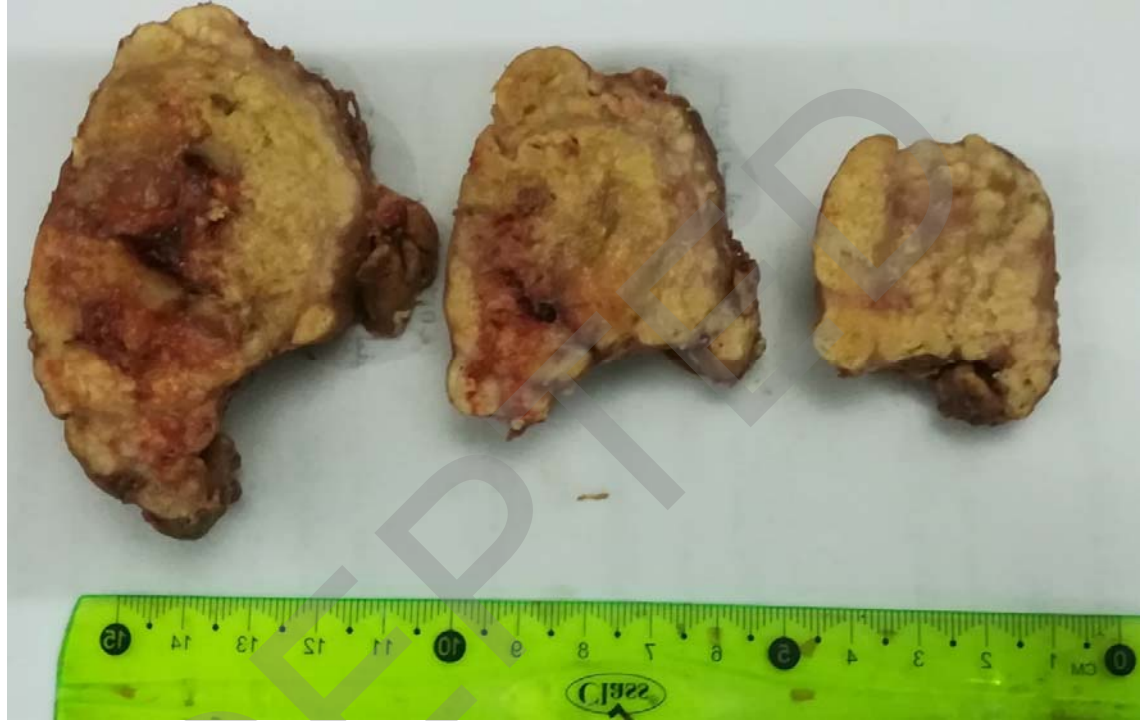
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Figure 1: Axial Computed Tomography with contrast of the thorax reveals increase in thyroid tissue size (4 cm x 3.5 cm). Its density is heterogeneous with the presence of necrotic areas and areas that enhance the contrast material in a heterogeneous manner in the arterial phase. This formation pushes the elements of the mediastinum and trachea to the right side.

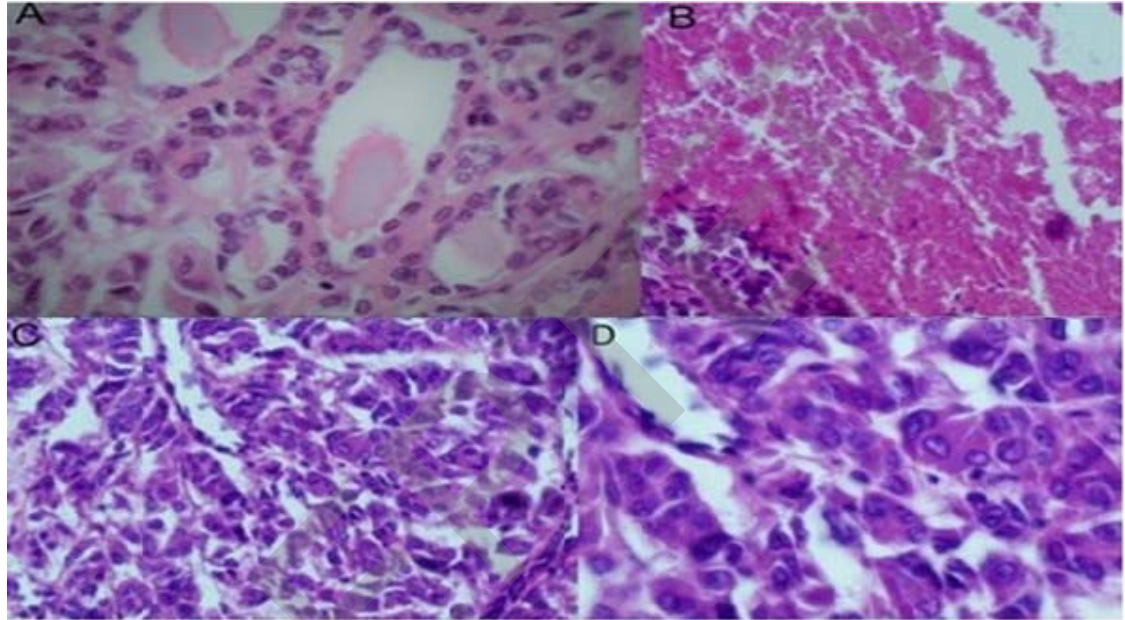


Figure 2: Macroscopic examination of the retrosternal goiter weighing 350g. The right lobe measured 5×4×4 cm, and the left lobe measured 13×8×7 cm, the cut sections of both lobes demonstrated ill-defined nodules of yellow-tan coloration with foci of central necrosis.



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Figure 3: Microscopic examination of the thyroid tissue. Variable-sized follicles full of colloid and lined by a single layer of normal cuboidal cells (A: H&Ex200), areas of necrosis (B: H&Ex100), and an infiltrative growth pattern of insular, trabecular, and solid formations of neoplastic epithelial cells with scant eosinophilic cytoplasm, hyperchromatic convoluted nuclei, and bizarre mitotic figures with areas of necrosis and hemorrhage (C: H&Ex200, D: H&Ex400).



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