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Poorly Differentiated Thyroid Cancer: Experience Of 9 Cases In The Nuclear Medicine Department Of CHU Hassan II Of Fez

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Abstract:
Background: *Poorly Differentiated Thyroid Carcinoma (PDTC) is a rare and aggressive form of thyroid cancer, representing 1% to 3% of all thyroid malignancies. This study evaluates the clinical, biological, and therapeutic characteristics of 9 patients treated at the Nuclear Medicine Department of CHU Hassan II in Fez. The aim is to analyze the efficacy of high-dose radioiodine therapy and alternative treatments in patients who exhibit iodine-131 refractoriness.*
Materials and Methods: *In this retrospective study, 9 patients diagnosed with PDTC and treated with high-dose radioiodine therapy were analyzed. Clinical parameters such as age, sex, metastasis at diagnosis, iodine refractoriness, and therapeutic response were evaluated. Patients refractory to radioiodine therapy were treated with sorafenib. Survival rates and follow-up outcomes were assessed over 24 months.*
Results: *The median age was 58 years, with a female predominance (67%). Initial metastases were present in 5 patients (55%). Three patients (33%) were refractory to iodine-131 and received sorafenib. The overall survival rate at 24 months was 89%. Despite aggressive therapies, radioiodine-refractory patients demonstrated poorer prognoses.*
Conclusion: *Poorly Differentiated Thyroid Carcinoma remains a challenging malignancy due to its aggressiveness and frequent iodine-131 refractoriness. High-dose radioiodine therapy is effective in selected patients, but targeted therapies such as sorafenib are crucial for refractory cases to improve outcomes.*
Keyword: *Poorly Differentiated Thyroid Cancer, Radioiodine Therapy, Metastases, Sorafenib, I-131 Refractoriness.*

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I. Introduction

Poorly Differentiated Thyroid Carcinoma (PDTC) is a rare and aggressive form of thyroid cancer, accounting for approximately 1% to 3% of all thyroid malignancies[1]. First described by Carcangiu et al. in 1984, PDTC represents an intermediate entity between well-differentiated thyroid carcinoma (WDTC) and undifferentiated or anaplastic carcinoma[2]. It retains some features of differentiation but lacks the favorable prognosis associated with WDTC, making early diagnosis and appropriate management crucial[3].

Histologically, PDTC is characterized by solid, trabecular, or insular growth patterns and demonstrates high mitotic activity, necrosis, and partial loss of typical thyroid markers[4]. The presence of these aggressive features contributes to its poorer prognosis compared to WDTC[5].

PDTC often presents at an advanced stage with a high rate of distant metastases, particularly to the lungs, bones, and liver[6]. Studies show that 30% to 50% of patients have distant metastases at diagnosis[7]. This metastatic potential, combined with frequent resistance to Iodine-131 therapy, complicates treatment and limits therapeutic options[8]. Consequently, patients often require a multimodal approach, including surgery, high-dose radioiodine therapy, external beam radiation therapy (EBRT), and systemic therapies such as tyrosine kinase inhibitors (TKIs) like sorafenib[9].

Radioiodine refractoriness, defined as the inability of metastatic lesions to uptake Iodine-131, occurs in a significant proportion of PDTC patients[10]. This refractoriness is associated with a worse prognosis, necessitating the use of targeted therapies and novel treatment approaches[11]. In recent years, sorafenib and lenvatinib have demonstrated efficacy in improving progression-free survival in radioiodine-refractory cases[12].

Given the complexity of PDTC management, a multidisciplinary approach involving endocrinologists, nuclear medicine specialists, oncologists, and surgeons is essential to optimize patient outcomes[13]. Early diagnosis, accurate risk stratification, and timely intervention with appropriate therapeutic strategies remain the cornerstone of improving survival rates in patients with PDTC[14].

Objective: The aim of this study is to thoroughly analyze the clinical and biological characteristics of patients with poorly differentiated thyroid carcinoma (PDTC). This analysis includes the evaluation of demographic factors (age, sex), histopathological data, tumor markers, and disease characteristics at the time of diagnosis, such as the presence of metastases and the status of Iodine-131 refractoriness.

Another aspect of the study focuses on assessing the therapeutic responses to high-dose radioiodine therapy in these patients. The parameters examined include the number of administered treatment cycles, the efficacy of the therapy in terms of tumor size reduction or disease stabilization, and the long-term clinical and biological response. Identifying patients who are refractory to Iodine-131 and analyzing the alternative therapeutic strategies implemented, such as the use of sorafenib, are also key components of this study.

The ultimate objective is to better understand the predictive factors of treatment response and to improve the overall management of patients with PDTC, with the goal of optimizing survival outcomes and quality of life.

II. Materials And Methods

We conducted a retrospective study on 9 patients diagnosed with poorly differentiated thyroid carcinoma (PDTC) in the Nuclear Medicine Department of CHU Hassan II in Fez.

The inclusion criteria for the study comprised a histologically confirmed diagnosis of PDTC based on biopsies and pathological analysis, along with treatment involving high-dose radioiodine therapy, defined as the administration of at least 100 mCi of Iodine-131. Patients included in the study were required to have regular follow-up with clinical and biological evaluations. Patients with other types of thyroid cancer or incomplete follow-up data were excluded from the study.

Data were collected from the patients' medical records. The information gathered included age at diagnosis, sex, initial symptoms, and tumor stage according to the TNM classification. The number of radioiodine therapy cycles administered, the presence and location of metastases, and the status of Iodine-131 refractoriness were also analyzed.

Patients who did not respond to Iodine-131 therapy were considered refractory. These patients were referred to the oncology department for targeted therapies such as sorafenib.

Regular clinical and biological follow-up was conducted for each patient. Clinical examinations were performed quarterly, while biological assays, including thyroglobulin and anti-thyroglobulin antibodies, were measured to monitor disease progression. The effectiveness of the treatment was determined based on disease stability, tumor reduction, or progression.

III. Results

Among the 9 patients included in this study, the median age at diagnosis was 58 years, with a range from 45 to 70 years. A female predominance was noted, with 6 women and 3 men affected. The most common presenting symptoms were palpable cervical nodules, observed in 67% of patients (6 patients), and persistent neck pain, reported in 33% of patients (3 patients). These clinical signs, among other symptoms, were common reasons for consultation and prompted further investigations. This diagnostic process eventually led to surgical intervention, followed by histopathological examination, which confirmed the diagnosis of poorly differentiated thyroid carcinoma.

At the time of diagnosis, 5 patients, representing 55%, had distant metastases. The metastases were primarily located in the lungs in 3 cases and in the bones in 2 cases. The presence of metastatic disease at diagnosis indicated an advanced tumor stage, necessitating aggressive therapeutic intervention.

All patients underwent high-dose radioiodine therapy. The median number of radioiodine therapy cycles administered was 3 cycles, with a range from 2 to 5 cycles. Despite this treatment, 3 patients were classified as radioiodine-refractory after evaluations demonstrated an absence of iodine uptake in the tumor sites. These patients were subsequently referred to the oncology department to receive treatment with sorafenib, a tyrosine kinase inhibitor. Sorafenib led to a partial improvement in symptoms and disease stabilization during the follow-up period.

The overall survival rate after a median follow-up of 24 months was 89%. Only one patient died due to rapid progression of metastatic disease, despite the treatments administered. This death underscores the aggressiveness of poorly differentiated thyroid carcinoma, particularly in patients with metastatic disease that is refractory to conventional therapies.

IV. Discussion

Our findings are consistent with the existing literature on poorly differentiated thyroid carcinoma (PDTC), highlighting its aggressive nature and frequent metastatic dissemination. In addition to the metastatic rate and radioiodine refractoriness discussed earlier, several other clinical and biological parameters observed in our study align with published data on PDTC.

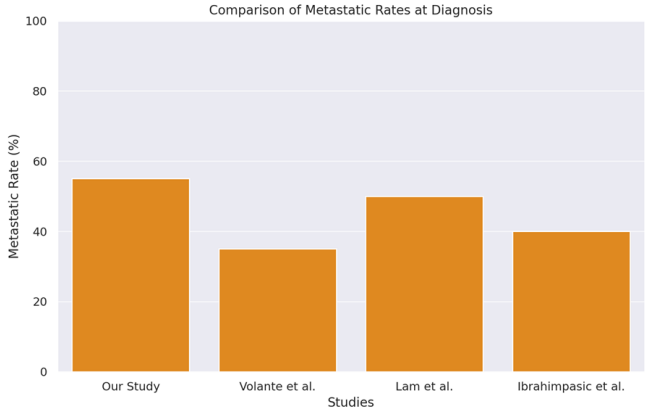
The median age of our patients, 58 years, is in line with findings from studies by Sakamoto et al., who reported that PDTC predominantly affects middle-aged and older adults, with a median age of 55 to 60 years[5]. This age distribution supports the notion that PDTC represents a transitional state between well-differentiated thyroid carcinoma and anaplastic thyroid carcinoma, which typically occurs in older patients[1]. The female predominance in our cohort (67%) also reflects the general trend observed in thyroid malignancies, where women are more commonly affected, as reported by Lam et al[6].

Symptomatology in our study, particularly the presence of palpable cervical nodules (67%) and persistent neck pain (33%), is consistent with other case series on PDTC. A study by Ibrahimpasic et al. noted that cervical masses and compressive symptoms are the most common presenting features, often signaling advanced disease[2]. These symptoms emphasize the need for early diagnostic interventions to prevent delayed diagnoses associated with worse outcomes.

In our study, 55% of patients presented with metastases at diagnosis. This rate aligns with findings by Volante et al., who reported metastatic rates ranging between 20% and 40% in patients with PDTC[5]. Similarly, Lam et al. found that up to 50% of PDTC patients exhibit distant metastases at the time of diagnosis, predominantly in the lungs and bones[1]. These high rates of metastatic spread underscore the need for comprehensive initial staging and a multidisciplinary approach to treatment.

Figure 1: Metastatic Rates at Diagnosis

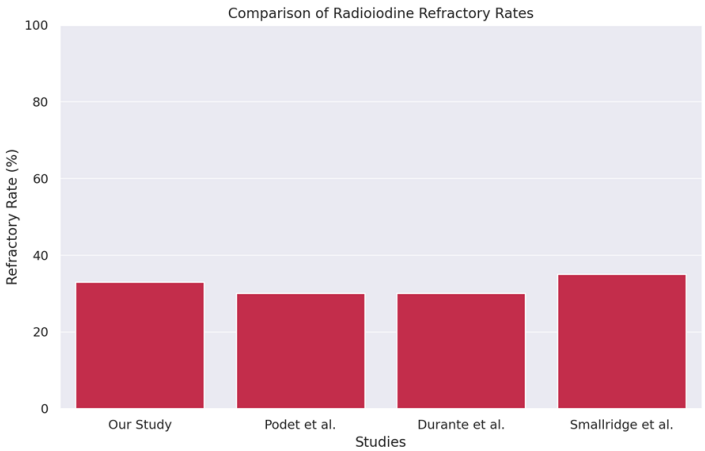
This figure shows that our study's metastatic rate (55%) aligns closely with other studies, underscoring the aggressive nature of PDTC and the importance of early comprehensive staging.



In terms of therapeutic response, the median number of radioiodine therapy cycles administered in our cohort was three, with a range of two to five cycles. This is comparable to the study by Durante et al., where patients with PDTC typically underwent multiple cycles of radioiodine therapy, although the response varied significantly depending on the degree of differentiation and iodine uptake[8]. The limited efficacy of radioiodine therapy in PDTC underscores the importance of alternative treatment modalities for patients with refractory disease.

Figure 2: Radioiodine Refractory Rates

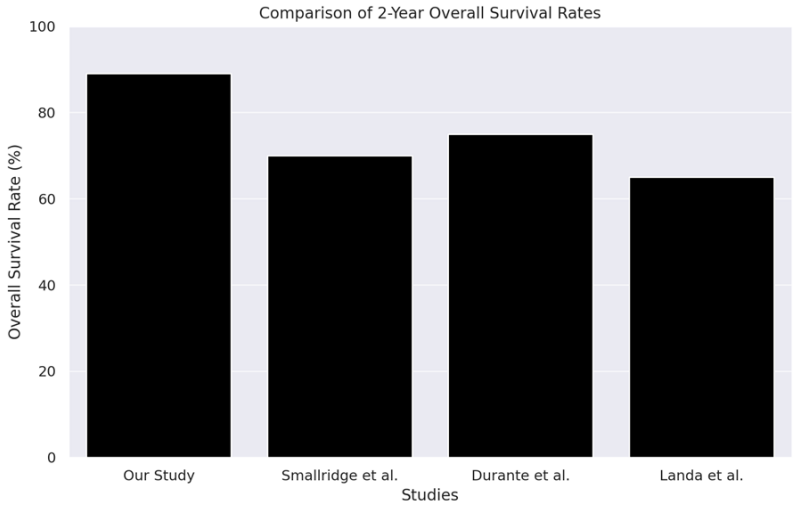
The refractory rate (33%) in our study is consistent with the rates reported by other studies, highlighting the frequent need for alternative therapies such as targeted treatments in PDTC management.



The overall survival rate in our study after a median follow-up of 24 months was 89%. This outcome is slightly higher than reported in larger series. For instance, Smallridge et al. reported a two-year survival rate of 70% in patients with PDTC, reflecting the heterogeneity of disease progression and the importance of individualized treatment strategies[15]. The relatively favorable survival rate in our cohort may be attributed to the multidisciplinary management approach and the early introduction of targeted therapies for refractory cases.

Figure 3: Year Overall Survival Rates

Our study's 2-year overall survival rate (89%) is higher compared to other studies, possibly reflecting the benefits of a multidisciplinary approach and early introduction of targeted therapies.



The absence of data on the BRAF mutation status, RAS mutations, and the Ki-67 proliferation index in our study is a notable limitation. These biomarkers are increasingly recognized as critical for prognosis and treatment decision-making. For example, the presence of BRAF V600E mutations has been associated with poorer outcomes and reduced iodine uptake in PDTC patients[16]. Similarly, a high Ki-67 index correlates with increased tumor aggressiveness and worse survival rates, as demonstrated by Volante et al[17]. Future studies should incorporate these molecular markers to improve risk stratification and guide targeted therapies.

Another important parameter not fully explored in our study is the use of external beam radiation therapy (EBRT). EBRT has shown potential in controlling locoregional disease and improving survival in patients with PDTC who are not candidates for surgery or radioiodine therapy[18]. The integration of EBRT into the treatment algorithm for PDTC patients with advanced disease warrants further investigation.

Additionally, the role of immunotherapy in PDTC is an emerging area of interest. Recent studies suggest that immune checkpoint inhibitors, such as pembrolizumab and nivolumab, may offer benefits in patients with refractory thyroid cancers, particularly those with high tumor mutational burden[19]. Combining immunotherapy with targeted therapies could provide a promising approach for managing PDTC in the future.

In conclusion, while our study provides valuable insights into the clinical and therapeutic characteristics of PDTC, incorporating molecular profiling, EBRT, and immunotherapy into future research will enhance our understanding and management of this challenging disease.

V. Conclusion

Poorly differentiated thyroid carcinoma (PDTC) remains a rare but aggressive malignancy that poses significant therapeutic challenges. Despite the essential role of high-dose radioiodine therapy, a substantial proportion of patients exhibit refractoriness to iodine-131, complicating disease management and prognosis[8]. In these cases, targeted therapies such as sorafenib have shown promise in improving progression-free survival and stabilizing disease[12]. The integration of these targeted agents has thus become an important component of the therapeutic arsenal for PDTC.

Advances in molecular profiling have underscored the importance of biomarkers such as BRAF mutations and the Ki-67 proliferation index in guiding personalized treatment approaches[16,17]. BRAF mutations have been linked to reduced radioiodine uptake and more aggressive tumor behavior, highlighting the need for individualized therapeutic strategies[20]. A high Ki-67 index has similarly been associated with poorer outcomes and more aggressive disease courses[6].

To improve patient outcomes, a multidisciplinary approach involving endocrinology, oncology, surgery, and nuclear medicine is essential[9]. Future research should focus on prospective studies that incorporate

molecular biomarkers and investigate novel therapeutic combinations, such as next-generation tyrosine kinase inhibitors and immunotherapy[19]. These efforts are crucial to advancing the understanding of PDTC and optimizing treatment strategies to enhance survival and quality of life for affected patients[7].

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