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LOCOREGIONAL RECURRENCES OF PAPILLARY THYROID CARCINOMA: A SINGLE-CENTER RETROSPECTIVE STUDY OF 6 CASES AND REVIEW OF PREDICTIVE FACTORS

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ABSTRACT

Background: Papillary thyroid carcinoma (PTC) has an excellent prognosis, but locoregional recurrences pose a significant therapeutic challenge. Identifying predictive factors is crucial for tailored management. **Objective:** To analyze the epidemiological, clinical, therapeutic, and evolutionary characteristics of locoregional recurrences of PTC and to identify associated risk factors. **Materials and Methods:** A single-center retrospective study (2010-2021) including 6 patients with a histologically confirmed locoregional recurrence of PTC out of 60 operated cases. **Results:** The recurrence rate was 10%. The mean age was 56.3 years with a sex ratio of 1. The median time to recurrence was 1 year. Recurrences were primarily lateral nodal (5/6 cases). Frequently identified factors included extrathyroidal extension (4/6), vascular invasion (3/6), and an initial tumor size ≥1cm (4/5 documented cases). Treatment consisted of surgical reintervention (5/6) combined with radioiodine therapy (RAI). The outcome was favorable in 3 cases. **Conclusion:** Despite an overall good prognosis, a significant proportion of PTC can recur. Complete and appropriate initial surgery, followed by rigorous surveillance based on thyroglobulin and ultrasound, is essential. The presence of risk factors such as ETE, vascular invasion, and large tumors should guide accurate risk stratification and close follow-up.

INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy, representing the majority of thyroid cancers. Its incidence is constantly increasing worldwide, primarily due to the diagnosis of microcarcinomas [1, 2]. Its prognosis is generally excellent, with 10-year survival rates exceeding 90% [3, 4]. Nevertheless, a non-negligible proportion of patients, estimated between 2.2% and 16.6% across series, develop locoregional recurrences (lymph node or in the thyroid bed) [5-7]. These recurrences significantly impact quality of life, morbidity, and require complex treatments.

Initial management (surgery, RAI) and surveillance (thyroglobulin (Tg) assay, ultrasound) are well codified by international guidelines (ATA, ETA) [8, 9]. The early identification of high-risk patients, based on prognostic factors such as age, tumor size, extrathyroidal extension (ETE), nodal involvement, and aggressive histological variants, is fundamental to adapting treatment and surveillance [10, 11].

Through this single-center retrospective study of 6 cases of locoregional recurrence of PTC, we aim to describe their characteristics and discuss predictive factors and management modalities, contrasting them with recent literature data

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MATERIALS AND METHODS

Study Design and Population: This was a retrospective descriptive study, conducted over a 10-year period (January 2010 - January 2021) in the ENT department of the Moulay Ismail Military Hospital in Meknes. Out of 1730 total thyroidectomies performed during this period, 60 cases of PTC were diagnosed. Six (6) patients with a histologically confirmed locoregional recurrence were included in the study.

Studied Parameters: The following data were collected from medical records:

- **Epidemiological data:** Age, gender, medical history.
- **Clinical data:** Circumstances of discovery of the initial tumor and recurrence.
- **Paraclinical data:** Results of ultrasound, thyroid biology (TSH, Tg, Anti-Tg antibodies), histopathology (histological type, size, ETE, vascular emboli, nodal

involvement), and advanced imaging (CT, MRI, PET-CT) if performed.

- **Therapeutic data:** Initial and salvage surgical procedures, RAI (I-131) doses, modalities of TSH-suppressive therapy.
- **Outcome data:** Time to recurrence, site of recurrence, response to treatment, final status.

Inclusion Criteria: Patients >18 years old managed for a histologically confirmed locoregional recurrence of PTC. **Exclusion Criteria:** Other histological types of thyroid cancer, isolated distant metastases without associated locoregional recurrence, incomplete records.

Ethical Considerations: Patient data confidentiality was strictly maintained.

Data Analysis: The analysis was descriptive. Quantitative data are presented as means or medians, and qualitative data as counts and percentages.

RESULTS

1. **Epidemiological Data:** Out of 60 operated PTCs, 6 locoregional recurrences were identified, yielding a **recurrence rate of 10%**. The mean age of patients at the time of recurrence diagnosis was **56.3 years** (range: 34-79 years). The distribution by age and gender was balanced (3 men, 3 women, sex ratio =1).

- **Graph 1:** Distribution of patients by age group (<35 years: 1; 35-45 years: 1; >45 years: 4).
- **Graph 2:** Distribution by gender (Male: 50%; Female: 50%).

2. **2. Table 1: Patient Characteristics and Initial Tumor Profile**

3. **Circumstances of Discovery and Recurrence Diagnosis** The initial tumor was discovered on thyroidectomy specimen for goiter in 4 cases. Recurrence was suspected due to **elevated Tg levels**(5/6 cases), isolated or associated with structural disease on ultrasound. One patient presented with isolated elevated Anti-Tg antibodies. PET-CT was crucial for localizing recurrence in 4 patients, particularly in cases of discordance between high Tg and negative iodine scintigraphy.

4. **Time to and Site of Recurrence** The **median time to recurrence** was **1 year** (range: 1-4 years). Recurrences were predominantly **lateral nodal** (5/6 cases), involving the jugulocarotid chains. Two cases combined local (thyroid bed) and regional recurrence.

5. **Recurrence Treatment and Outcome** Five patients (83.3%) underwent **surgical reintervention** (neck dissections). Adjuvant RAI was administered in all cases. TSH-suppressive therapy (TSH <0.1 mUI/L) was maintained or intensified. The outcome was favorable (biochemical and structural remission) in 3 patients. One patient had persistent disease (elevated Tg, residual lymph nodes). Two patients developed distant metastases (pulmonary, bone, cerebral).

DISCUSSION

Our study, although based on a limited sample, found a **recurrence rate of 10%**, consistent with literature reporting rates ranging from 2.2% to 16.6% [5-7, 12]. The short median time to recurrence (1 year) underscores the importance of close surveillance during the first years.

The **predominance of lateral nodal recurrences** (83.3%) contrasts with older series reporting a central compartment predominance [13] but aligns with recent data [14]. This shift could be explained by the more systematic performance of initial prophylactic central neck dissection, moving the recurrence site to lateral compartments, and by the phenomenon of "skip metastases" (lateral involvement without central involvement)

Case	Age*	Sex	Size (cm)	Multifocality	ETE	Nodal Involv.	Histological Type	Vascular Invasion	ATA Risk Stage
1	47	F	NA	No	Yes (Macro)	No	Follicular Variant	No	Intermediate
2	34	M	2.0	No	No	No	CPTC	Yes	Intermediate
3	29	M	1.0	No	Yes (Micro)	Yes	CPTC	No	Intermediate
4	73	F	5.0	Yes	Yes (Macro)	No	Follicular Variant	Yes	High
5	51	M	NA	No	No	No	CPTC	No	-
6	63	F	1.5	Yes	Yes (Macro)	Yes	CPTC	Yes	High

Age at initial diagnosis. NA: Not Available; ETE: Extrathyroidal Extension (Micro: Minimal; Macro: Gross); CPTC: Conventional Papillary Thyroid Carcinoma.

[15].

The analysis of **risk factors** in our series aligns with established data. **Extrathyroidal extension (ETE)** was present in 4 out of 6 cases, confirming its major adverse prognostic role, especially in its gross form [16, 17]. **Vascular invasion**, an independent risk factor for recurrence and distant metastasis [18], was found in 3 patients. A **tumor size ≥1 cm** was noted in 4 of the 5 patients for whom this data was available. While multifocality and initial nodal involvement were less constant, their presence should raise concern [19, 20].

The **Tg assay** confirmed its role as the cornerstone of surveillance, with its elevation being the main mode of recurrence detection [8, 9]. **PET-CT** proved crucial in cases of non-iodine-avid residual disease (high Tg, negative scintigraphy), with high sensitivity for locating recurrences, as demonstrated by several studies [21, 22].

The management of recurrences relies primarily on **salvage surgery** when the lesion is accessible and resectable, as was done for 5 of our patients. This procedure must be as complete as possible to optimize cure chances [23]. **Adjuvant RAI** remains an essential therapeutic adjunct, even if its benefit is better established for advanced diseases [8,24]. **TSH-suppressive therapy** (TSH <0.1 mUI/L) is recommended in this context of persistent disease [8].

The limitations of our study are its retrospective nature, the small sample size, and the lack of molecular marker testing (BRAF, TERT). A prospective study including a larger cohort and genetic analysis would refine risk stratification.

CONCLUSION

This study confirms that locoregional recurrences of PTC, although infrequent, constitute a significant clinical entity. Optimal and complete initial surgery (total thyroidectomy + lymph node dissection adapted to nodal status) is the best preventive strategy. Post-operative surveillance must be rigorous and prolonged, based on serum Tg assay and cervical ultrasound, reserving PET-CT for discordant situations. Identifying initial risk factors (ETE, vascular invasion, large tumor size) allows for targeting patients requiring closer follow-up. The management of recurrences must be multidisciplinary, prioritizing salvage surgery whenever possible.

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