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Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features at the University Hospital Center Joseph Ravoahangy Andrianavalona, Antananarivo

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ABSTRACT

Introduction: *Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a recently recognized entity introduced in the 2017 WHO classification because of its indolent behavior and excellent prognosis. Data from Madagascar remain limited. This study aimed to describe the epidemiological and histopathological features of NIFTP in the study setting.*

Materials and Methods: *A retrospective descriptive study was conducted at the Department of Pathology of the University Hospital Center Joseph Ravoahangy Andrianavalona (CHU-JRA) over a 5-year period, from January 2020 to December 2024.*

Results: *During the study period, 20 cases of NIFTP were identified, accounting for 6% of thyroid lesions and 27.7% of papillary thyroid carcinomas. The mean age of patients was 38 ± 12 years, ranging from 16 to 69 years. A marked female predominance was observed, with a sex ratio of 0.18. Total thyroidectomy was performed in 60% of cases. Macroscopically, in 55% of cases, the lesion presented as a single, well-encapsulated nodule measuring 0.2 to 10 cm. Histologically, the tumors showed a microfollicular or macrofollicular architecture associated with papillary-type nuclear atypia, without significant papillary architecture or capsular and vascular invasion.*

Conclusion: *NIFTP is a thyroid entity with low malignant potential and an excellent prognosis. Its diagnosis relies on strict histopathological criteria, allowing conservative management and reducing overtreatment of patients.*

Keywords

Histopathology, Madagascar, NIFTP, Papillary carcinoma, Thyroid.

Introduction

Papillary carcinoma accounts for more than 90% of newly diagnosed thyroid cancers [1]. Some entities previously classified within this group have recently been reconsidered because of their indolent biological behavior, including non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), a new entity introduced by the WHO in 2017 [1]. Its recognition as a distinct entity is important because the survival rate approaches 100%, with an almost negligible risk of recurrence [2]. Following this reclassification, several Western series reported a reduction in the incidence of papillary thyroid carcinoma estimated at 10–20% [3]. However, data from developing countries such as Madagascar remain scarce, highlighting the relevance of the present study. The aim of this study was to describe the epidemiological and

histopathological characteristics of NIFTP in the study setting.

Materials and Methods

This was a retrospective descriptive study of thyroid NIFTP lesions diagnosed at the Department of Pathology of the University Hospital Center Joseph Ravoahangy Andrianavalona (CHU-JRA), Antananarivo, over a 5-year period from January 2020 to December 2024.

Results

During the study period, 20 cases were identified, representing 6% of thyroid lesions and 27.7% of papillary thyroid carcinomas.

Age

The mean age of patients was 38 ± 12 years, ranging from 16 to 69 years, with predominance in the 15–30-year age group (Figure 1).

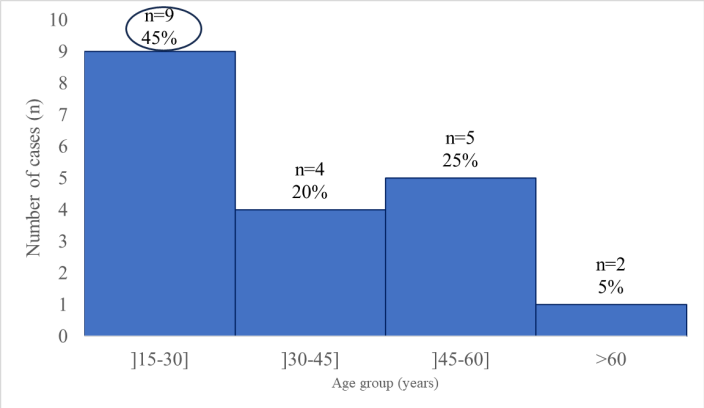

Figure 1: Distribution of patients according to age groups.

Gender

A marked female predominance was observed, with a sex ratio of 0.18 (Figure 2).

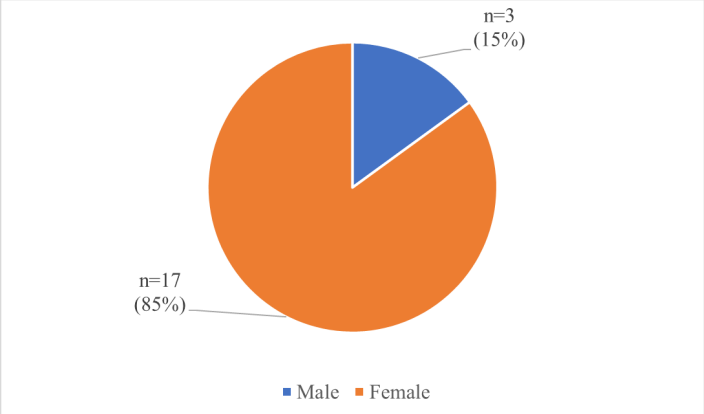

Figure 2: Distribution of patients according to gender.

Type of specimen

Total thyroidectomy was performed in 60% of cases.

Type of specimen	Number (n=20)	Percentage (%)
Lobectomy	8	40
Total thyroidectomy	12	60

Anatomopathological findings

Macroscopically, in 11 cases (55%), the lesion presented as a single, well-encapsulated nodule measuring 0.2 to 10 cm in greatest dimension, whereas the remaining 9 cases were associated with multinodular goiter.

Histological examination showed well-circumscribed nodules clearly demarcated from the adjacent thyroid tissue by a thin fibrous capsule. The lesions consisted of thyroid follicles displaying microfollicular or macrofollicular architecture and lined by cells exhibiting the nuclear features of papillary thyroid carcinoma. No papillary architecture was identified. These findings allowed the diagnosis of non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in all cases (Figure 3).

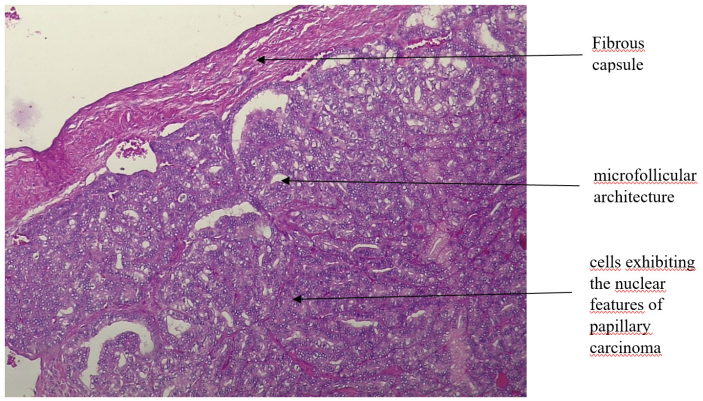

Figure 3: Lobectomy specimen: NIFTP
Coloration: Hematoxylin and eosin stainingx100; Magnification x100
Source: Department of Pathology

Discussion

Until 2016, NIFTP was classified as a subtype of papillary thyroid carcinoma and was designated as non-invasive encapsulated follicular variant of papillary thyroid carcinoma. Its frequency ranges from 9% to 22% among papillary carcinoma variants [4]. The reclassification proposed by Nikiforov YE et al. [2] represented a major turning point, based on evidence demonstrating the absence of recurrence and metastasis after long-term follow-up. This observation and the need for reclassification were also supported by Thompson DR in a study involving 94 cases of encapsulated papillary carcinoma [5]. Consequently, the term NIFTP was introduced in the 2017 WHO classification, where it is now recognized as a distinct entity among encapsulated follicular tumors [1]. The lesion was described as non-invasive because of the presence of a surrounding capsule and the absence of invasion into adjacent thyroid tissue or metastasis.

NIFTP is an uncommon lesion, accounting for approximately 9.1% of all papillary thyroid carcinomas worldwide. It is particularly

rare in Asian populations (1.6%) compared with Western series (13.3%) and has occasionally been reported in pediatric populations [6,7]. In the present study, NIFTP represented 6% of all thyroid lesions diagnosed in the department and 27.7% of papillary thyroid carcinomas.

From a molecular perspective, NIFTP is commonly associated with mutations in the RAS family genes [8], particularly *NRAS*, and less frequently *HRAS* and *KRAS*, with reported frequencies ranging from 36% to 67% [9]. This molecular profile distinguishes NIFTP from classical papillary thyroid carcinoma, which is more commonly associated with *BRAF* mutations, and supports its classification among lesions with low malignant potential. Therefore, NIFTP is currently regarded as a borderline or even precancerous lesion rather than a frankly malignant tumor [2].

Macroscopically, the nodules are typically solid, well-circumscribed, and encapsulated [1]. The average tumor size ranges from 2 to 3 cm, varying from a few millimeters [10] up to 8 cm [11]. Xu B et al. reported that, similar to smaller lesions, large NIFTPs (≥4 cm) do not appear to carry any risk of recurrence, even when managed conservatively [11]. In the present study, tumor size was consistent with previously reported data (0.2–10 cm), and all nodules were encapsulated.

The diagnosis of NIFTP relies on strict histopathological criteria. It requires a follicular growth pattern associated with the nuclear features of papillary thyroid carcinoma and a well-circumscribed lesion that may be encapsulated [2,12]. In the present series, all nodules were well encapsulated. The diagnosis was established according to the morphological criteria described by Nikiforov YE et al. [2]. It is important to emphasize that no preoperative method alone can definitively establish the diagnosis of NIFTP. According to Pusztaszeri M et al. [9], the combination of cytological, ultrasonographic, and molecular findings may suggest the possibility of NIFTP or exclude it in favor of classical papillary thyroid carcinoma; however, definitive diagnosis requires complete histological examination of the surgical specimen.

The nuclear score used for NIFTP corresponds to the system proposed by Nikiforov YE et al. [2] and adopted by the WHO to assess papillary-type nuclear atypia. It is based on three groups of nuclear features. Each group is scored 0 if absent and 1 if present. These include nuclear size and shape abnormalities (enlargement, overlapping, elongation), irregularities of the nuclear membrane (irregular contours, grooves, pseudoinclusions), and chromatin characteristics (clearing with margination and glassy nuclei). To assign a score of 1 to a group, not all abnormalities need to be present; the identification of at least one convincing abnormality within the group is sufficient. A total score of 2–3 is required for the diagnosis of NIFTP. In addition, the absence of capsular or vascular invasion is mandatory, as is the absence of significant papillary architecture, which should not exceed 1% of the tumor surface. Therefore, complete examination of the tumor capsule is essential to exclude any invasion [2]. In the present study, all cases fulfilled these diagnostic criteria, with well-encapsulated lesions lacking vascular or capsular invasion.

From an evolutionary standpoint, NIFTP is associated with an excellent prognosis, as demonstrated in the study by Nikiforov YE et al. [2], which included 109 patients with non-invasive follicular variant of papillary thyroid carcinoma followed over 13 years. Therapeutically, NIFTP differs from conventional thyroid carcinoma by allowing conservative management. Limited surgical excision, particularly lobectomy, is generally sufficient. It also enables exclusion of invasive follicular variant papillary thyroid carcinoma, classical papillary thyroid carcinoma, or any other malignant thyroid tumor [13]. Additional treatments such as total thyroidectomy and radioactive iodine therapy are not indicated in the absence of aggressive features. In the present series, no adjuvant treatment was administered after confirmation of the diagnosis, and patients underwent simple clinical follow-up. The recognition of NIFTP as a distinct entity has had a major impact on clinical practice. The removal of the term “carcinoma” aims to reduce overdiagnosis and overtreatment, limit complications related to unnecessary therapies, and decrease healthcare costs. This approach is consistent with a more rational and personalized management strategy for thyroid nodules.

Conclusion

NIFTP is a distinct thyroid entity characterized by indolent behavior and an excellent prognosis. Its diagnosis relies on rigorous histopathological evaluation based on the identification of precise morphological criteria and the exclusion of any invasion. This reclassification has significantly modified patient management by promoting conservative therapeutic strategies and avoiding overtreatment.

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