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Case Report

What psammoma bodies can represent in the thyroid. What we recently learnt from a story of lack of evidence

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Summary
The detection of psammoma bodies (PBs) in the thyroid gland is commonly associated to classic papillary thyroid carcinoma (PTC) and are frequently encountered in differnt subtypes of PTCs. Nonetheless, the evidence of PBs without a PTC may represent a diagnostic challenge. The general statement is that PBs represent a metastatic finding of PTC either when encountered inside the thyroid parenchyma or in the perithyroidal lymph nodes. The majority of authors assess that in presence of PBs, a search for an occult PTC is strongly encouraged and mandatory, especially if a lobectomy had been performed. In fact, it is not uncommon that a contralateral or ipsilateral tumor, mostly PTC, is found leading to the suggestion that the best recommendation is to submit the entire thyroid tissue. Nonetheless, when a cancer has not been found, the possibility of the rare evenience that PBs are likely to be associated with benign conditions should be considered among the differential diagnosis. Herein a short commentary and review of the literature on PBs detection and its diagnosis, based on our recent experience.

Key words: thyroid carcinoma, psammoma bodies, papillary thyroid carcinoma, Hashimoto thyroiditis

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Case history

In June 2022 a 74-year-old woman was admitted to the hospital for a total thyroidectomy with a history of multinodular goiter pressing on the trachea. Laboratory examination, including thyroid hormones, showed elevated TgAB and TPO levels, demonstrating the clear clinical evidence of a thyroiditis. The patient did not undergo a fine needle aspiration cytology (FNAC). The patient underwent a total thyroidectomy. The macroscopic evaluation revealed a 65 gm thyroid with a diffuse pseudonodular and adenomatous appearance. The histological samples confirmed a diffuse and severe bilateral lymphocytic Hashimoto thyroiditis with nodular oncocytic metaplasia (Fig. 1). Nonetheless, as an unexpected additional finding, there were multiple PBs in both thyroid lobes, in the absence of an obvious PTC or a possible sclerosing subtype of PTC (Figs. 2a-2b). The PBs were randomly distributed and they were at around 20-25 in number. The detection of a possible PTC was accurately studied. In fact, we decided to include all the thyroid tissue with the evaluation of multiple cut-levels. Further evaluation did not confirm any evidence of PTC. Hence, the performance of immunohistochemistry for HBME-1, galectin-3 and CK-19 on mulitple bilateral specimens from both lobes, was negative in each of them. The surgeons confirmed the removal of the en-

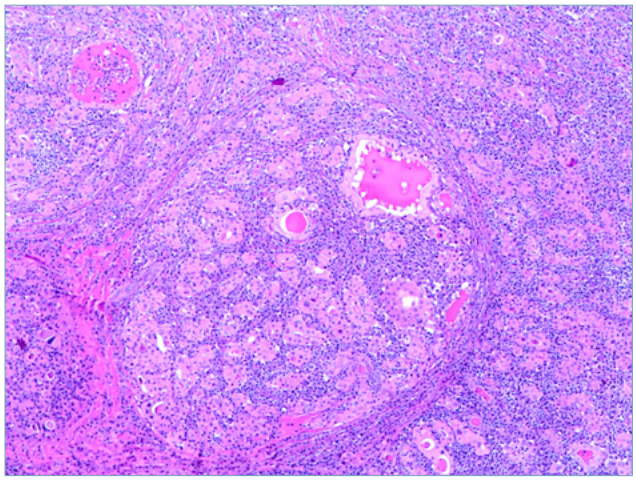

Figure 1. Histological evidence of Hashimoto thyroiditis and oncocytic metaplasia (H&E 200x).

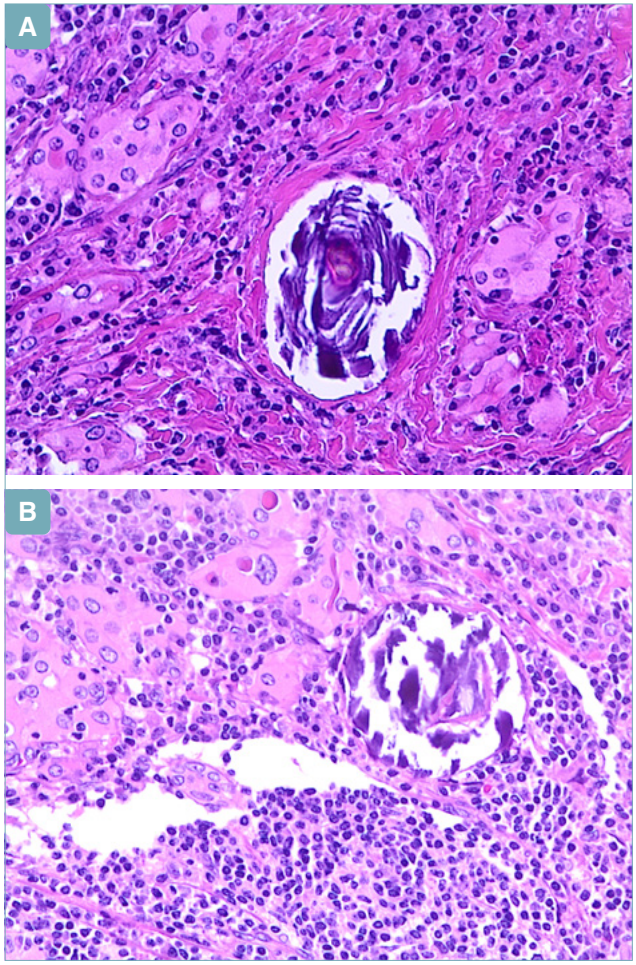

Figure 2. Histological evidence of psammoma bodies detected in the context of Hashimoto thyroiditis. The two pictures are from 2 different points in the thyroid parenchyma (H&E 200x).

tire thyroid tissue, without any macroscopic evidence of residual thyroid tissue. The conclusive diagnosis was in favor of a pseudonodular hyperplastic oncocytic metaplasia in a severe and diffuse background of chronic lymphocytic Hashimoto thyroiditis. Due to the presence of several PBs we added a note, describing the incidental detection of PBs in the confirmation of the lack of any PTC. We suggested a strict clinical follow-up for the patient. The lesson learnt from this case is that PBs are not always associated with PTC, even though a PTC is the first diagnosis to be excluded.

Discussion

The majority of authors consider PBs as a clear diagnostic feature of PTC [1-5]. According to the morphological features, PBs are round to oval calcification with a typical lamellation. Their origin has been debated and mostly linked to either the possibility of thrombosis in the papillary fibrovascolar core or the necrotic evolution of a lymphatic metastasis [2]. It takes for granted that, according to these definitions, PBs are strongly associated with a thyroid carcinoma. In fact, PBs are frequently encountered in the context of PTCs as well as in some of its subtypes, in which they are an important diagnostic finding (i.e diffuse sclerosing subtype of PTC). To note, the latter subtype is frequently encountered in young patients, and is characterized by diffuse bilateral involvement of the gland, lymphovascular invasion, extensive squamous metaplasia, abundant psamomma bodies, marked stromal fibrosis, and prominent lymphocytic infiltration. All these latter morphologic features were not seen after accurate evaluation of our case [3]. Nonetheless, PBs without evidence of a PTC are likely to pose several issues for their interpretation. To date, the majority of authors agreed that even if PBs can be encountered in few benign conditions and should be considered an extremaly rare occurence with, in any case, the suggestion of excluding an occult papillary carcinoma [1]. In a paper by Hunt et al., the authors described the clinical, pathological and follow-up data from 29 patients with PBs, without the detection of a thyroid carcinoma [1]. According to their results, in 27 of 29 cases there was a PTC after an accurate inclusion of the entire thyroid tissue, while the 2 remaining cases had no evidence of malignancy. In their analysis, the authors emphasized that these two latter patients underwent only a lobectomy, so that a complete inclusion and evaluation of the entire thyroid tissue had not been provided [1].

Despite this strong association between PBs and thyroid carcinomas, it is not uncommon that the detection

of only PBs is likely to pose some diagnostic dilemma. Are the PBs always and univocally associated with a diagnosis of PTC? Might we have some doubts about an occult PTC when we do not identify any malignant cell in the slides? And mostly, what do we have to do if PBs are found in a lobectomy? The current commentary originated from our recent and intriguing histological case that gave us the opportunity to think about the possible different meanings and significance of PBs. In our case, we included the entire thyroid tissue, with multiple levels without finding any evidence of classic PTC or any PTC subtype. The accurate search for any foci of carcinoma was negative.

The paper by Hunt et al. stressed the idea that non-tumor-associated PBs represent a metastatic thyroid disease, whether they are intraglandular or perithyroidal [1]. We agree with the authors that the detection of PBs is mandatory for submission of the entire thyroid specimens to find an occult PTC, and that any attempt should be directed to rule out a PTC. In fact, even though in the majority of cases an occult PTC is discovered, there are few cases in which a PTC is not detected and PBs can be associated with other benign conditions, as in our case and a few others, documented in the literature.

Specifically, to the best of our knowledge, our case is not the sole example. In fact, in a previous editorial, Lv et al. described a case of lymphocytic thyroiditis with multifocal non-tumor-associated PBs [5]. Furthermore, Triggiani et al., in their review article, assessed that 5% of benign thryoid lesions, including goiters and adenomas, showed PBs [4].

In a review article, Ferreira et al. emphasized that the major highlight is based on the suggestion to discriminate PBs from other types of micro and macro-calcifications in the contest of thyroid lesions [2]. In fact, they provided a detail analysis of all the different types of calcification, including PBs and inspissated colloid calcified, or stromal micro and macrocalcification. The pathognomonic features of PBs can be identified in the typical concentric lamelation and the lack of birefringence. These latter finding are absent in oxalate crystals and other calcifications in the contest of thyroid tissue. According to these morphological criteria, our case confirmed the morphological features of PBs. Despite the extremaly accurate search of an occult PTC, which was not detected in our samples, we concluded that PBs are likely to be associated with a benign condition such as Hashimoto thyroiditis. Our only bias is the absence of any lymph node removed by the surgeons, which was not possible to evaluate.

In conclusion, we can consider that thyroid cancer, and especially PTC, shows several types of calcification processes and PBs, which might be easily linked to a thyroid cancer in all cases in which a cancer is identified. Nevertheless, it also important to underline that PBs, in rare cases, might pose some difficult diagnostic issues. The role and significance of them is not completely clear, and mostly, can be associated with benign condition, as a diagnosis of exclusion. In presence of PBs, it is essential to make all attempts to exclude a PTC, even though the presence of PBs in benign thyroid lesions has been documented.

The authors hope that others will share their experience with the detection of PBs in thyroid benign conditions, so that the finding could be studied and confirmed in larger series as a possible diagnostic finding.

Conflict of interest

The authors declared no conflicts of interest.

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Ethical consideration

This manuscript was written in accordance with Declaration of Helsinki. Because this manuscript is only a retrospective description of a single case, an ethics committee approval was not necessary. Of course, we also obtained informed consent from the patient to publish the data.

Author contributions

EDR: conceptualization, formal analysis, operation, writing original draft, editing. LC: writing, review, editing. FP writing and editing. PT: methodology, editing. VF: review, editing.

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