A Case of Ovarian NIFTP Treated with Iratherapy

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Abstract

Struma ovarii is a form of mature monodermal teratoma, a rare germ cell tumor containing more than 50% thyroid tissue. Its transformation into a malignant tumor is rare. NIFTP (non-invasive follicular thyroid neoplasm with papillary nuclear features) is an entity characterized by a completely encapsulated follicular proliferation with papillary nuclear features, but without invasion or high-risk criteria. It has an excellent prognosis when located in the thyroid gland. Its presence in the struma ovarii makes its prognosis uncertain. We report a case of ovarian NIFTP treated with complementary iodine-131 isotope therapy.

The patient was a 50-year-old woman who consulted for a pelvic mass appearing on pelvic ultrasound as a large, double-component, cystic and fleshy mass measuring 109×100 mm. Pelvic CT scan, performed in addition to pelvic ultrasound to better assess the characteristics of the mass, revealed a solid-cystic pelvic mass affecting the left ovary, measuring 106x117×74 mm. Left adnexectomy was indicated based on these results. The pathological examination of the surgical specimen concluded that it was a NIFTP developed on a struma ovarii. A total thyroidectomy was performed. Histology concluded lymphocytic thyroiditis against a background of multi-hetero-nodular thyroid hyperplasia, with the presence of a follicular adenoma. She underwent complementary iratherapy treatment at 1.11 GBq.

The originality of this observation lies in the rarity of this histopathological entity, and the lack of international consensus on treatment opens the way for an approach aimed at codifying the classification, treatment protocol, and prognosis of ovarian NIFTPs.

Keywords: *struma ovarii; ovarian NIFTP; iratherapy*

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Introduction

Struma ovarii is a form of mature monodermal teratoma, a rare germ cell tumor containing more than 50% thyroid tissue [1]. Its transformation into a malignant tumor is rare [2]. Non-invasive follicular thyroid neoplasm with papillary nuclear features (NIFTP) is an encapsulated or clearly defined, noninvasive tumor with a follicular arrangement and nuclear features of papillary thyroid carcinoma (PTC), but without well-formed papillae or psammomatous bodies, and without the typical signs of aggressive subtypes of PTC or poorly differentiated carcinoma [3]. This lesion is considered "borderline" or "pre-malignant" [4]. The presence of NIFTP in a struma ovarii is an exceptional entity, described only twice in the literature [5]. To our knowledge, no author has yet addressed the value of complementary iratherapy in the management of ovarian NIFTP. We present a case of ovarian NIFTP in a woman in her fifties who had received iratherapy treatment in the nuclear medicine department of the Hassan II University Hospital in Fez.

Being individualized: Iodine therapy may be justified in the presence of risk factors or uncertainties regarding progression, particularly with the aim of optimizing prognosis and preventing recurrence. The case we have reported highlights the importance of an international registry and multicenter studies to define harmonized recommendations for the management of this extremely rare entity [6].

Case presentation

This is a 50-year-old female patient, third pregnancy, third delivery, with no history of radiation exposure during childhood, no family history of goiter, and no other notable medical or surgical history, who consulted for a pelvic mass unrelated to pregnancy. A pelvic ultrasound performed as part of the investigation of the mass revealed

the presence of a large, dual-component cystic and fleshy mass measuring 109×100 mm on the left ovary. To better assess the characteristics of this mass and its relationship to neighboring organs, a pelvic CT scan was performed. This confirmed the presence of a solid-cystic pelvic mass measuring 106x117×74 mm in the same location, with no other abnormalities detected. She underwent a left adnexectomy, the pathological examination of which was consistent with a NIFTP developed on a struma ovarii (Figures 1 and 2). PCR sequencing confirmed the presence of the C.1801 A>G. p. K601E mutation in exon 115 of the BRAF gene (Figure 3). Furthermore, the thyroid ultrasound was normal. The patient underwent a total thyroidectomy, the pathological examination of which was consistent with lymphocytic thyroiditis against a background of multi-hetero-nodular thyroid hyperplasia, with the presence of a follicular adenoma. She was therefore referred to the nuclear medicine department for further treatment with iodine therapy.

Given this clinical picture and ultrasound findings showing a thyroid gland that appeared essentially normal, a diagnosis of NIFTP developed on a struma ovarii was made. The patient underwent ablative radioiodine therapy at 1.11 GBq six weeks after total thyroidectomy. The peri-radioiodine therapy assessment performed during defrenation noted a well-stimulated ultrasensitive thyroestimulin (TSHus) at 116.1 mIU/L; tumor marker levels were 2.65 ng/mL for thyroglobulin (Tg) and anti-thyroglobulin antibodies (anti-Tg Ab) were positive at 21.7.
The whole-body scan with iodine-131 performed on day 3 after the iodine-131 treatment found two areas of iodine uptake in the thyroid bed (Figure 4) associated with thyroid remnants (Figures 5a and b), with no other areas of pathological uptake, particularly in the pelvic region. The post-treatment course following radioactive iodine-131 therapy was favorable. The patient was declared "cured" on the basis of satisfactory morphological, functional, and biological criteria: a low thyroglobulin level during perithyroid therapy, whole-body scanning with iodine-131 showing two thyroid remnants, and a cervical ultrasound scan 4 months after total thyroidectomy showing no abnormalities. She is currently receiving lifelong hormone therapy with L-thyroxine at a suppressive dose and undergoes annual clinical and biological monitoring.

Discussion

NIFTP is a newly defined, low-risk tumor entity [7]. It is characterized by a completely encapsulated follicular proliferation with papillary nuclear features, but without invasion or high-risk criteria. It has an excellent prognosis when located in the thyroid gland [3]. In this context, the standard treatment is generally limited to lobectomy without the need for radioiodine therapy or other adjuvant treatments, the aim being to avoid overmedicalization of indolent forms [8].

However, in the context of NIFTP developed on a struma ovarii, little data is available in the literature. The therapeutic approach therefore remains controversial due to the exceptional nature of this location and the lack of long-term follow-up data [9]. Our patient underwent a left adnexectomy and total thyroidectomy, followed by complementary iratherapy treatment at 1.11 GBq. This was due, on the one hand, to the uncertainty surrounding the biological behavior of NIFTP in the ovary; and on the other hand, the presence of risk factors such as tumor size not indicated by the pathologist and the presence of specific molecular alterations, in particular the C. 1801 A>G. p. K601E mutation in exon 115 of the BRAF gene.

Furthermore, there is currently no international consensus or published recommendations regarding the indication for iratherapy in this specific case. Most authors recommend a multidisciplinary approach, considering the individual profile of the patient, including age, comorbidities, the molecular specificity of the tumor, and local extension [5, 10]. What appears to be the first case of NIFTP within a struma ovarii was diagnosed at the Fernando Fonseca Hospital in Portugal and reported at the European Congress of Endocrinology in Milan, Italy, in 2022 [10]. The patient was a 32-year-old woman admitted to the emergency department with acute painful abdominal distension, in whom a well-defined right ovarian NIFTP measuring 1 cm in diameter was found. She had no associated thyroid ultrasound or histopathological abnormalities and had not received additional treatment with radioactive iodine-131.
In terms of follow-up, it is advisable to monitor patients clinically, radiologically, and by measuring thyroglobulin levels over the long term in order to detect local or distant recurrence at an early stage, even though the risk remains theoretically low due to the indolent nature of NIFTPs [11].
In the case we are reporting, the patient was declared "cured" based on satisfactory morphological, functional, and biological criteria, then placed on a suppressive dose of L-thyroxine with a target of 0.3< TSHus < 2, as she was classified as having a low risk of tumor recurrence according to the 8th edition of the UICC/AJCC classification. She is under clinical and biological sur-

veillance and undergoes annual ultrasound scans according to clinical guidelines.

According to some authors, complementary treatment with radioiodine therapy should be reserved for cases presenting risk criteria such as association with classic thyroid carcinoma, large ovarian NIFTP, or in cases of doubt about invasion or in the presence of molecular alterations (BRAF mutation) [12]. In the absence of consensus, the choice of therapeutic adjunct with radioactive iodine-131 in our patient was essentially based on a "precautionary" approach, given the absence of an indicated size for the ovarian NIFT and also the presence of the C. 1801 A> G. p. K601E mutation in exon 115 of the BRAF gene during sequencing by Polymerase Chain Reaction (PCR).

Conclusion

NIFTP developing on struma ovarii is an exceptional entity, with only two cases reported worldwide. Although thyroid NIFTP has an excellent prognosis, its progression in the ovarian context remains uncertain. In the absence of consensus, the management of ovarian NIFTP must be individualized. Iodine therapy may be justified in the presence of risk factors or uncertainties regarding progression, particularly with the aim of optimizing prognosis and preventing recurrence. The case we have reported highlights the importance of an international registry and multicenter studies to define harmonized recommendations for the management of this extremely rare entity.

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Declarations

Consent for publication: The author clarifies that written informed consent was obtained and the anonymity of the patient was ensured. This study submitted to Swiss J. Rad. Nucl. Med. has been conducted in accordance with the Declaration of Helsinki and according to requirements of all applicable local and international standards. All authors contributed to the conception and design of the manuscript, participated in drafting and revising the content critically for important intellectual input, and approved the final version for publication. Each author agrees to be accountable for all aspects of the work, ensuring its accuracy and integrity.
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Conflict of interest:

The authors declare that there were no conflicts of interest within the meaning of the recommendations of the International Committee of Medical Journal Editors when the article was written.

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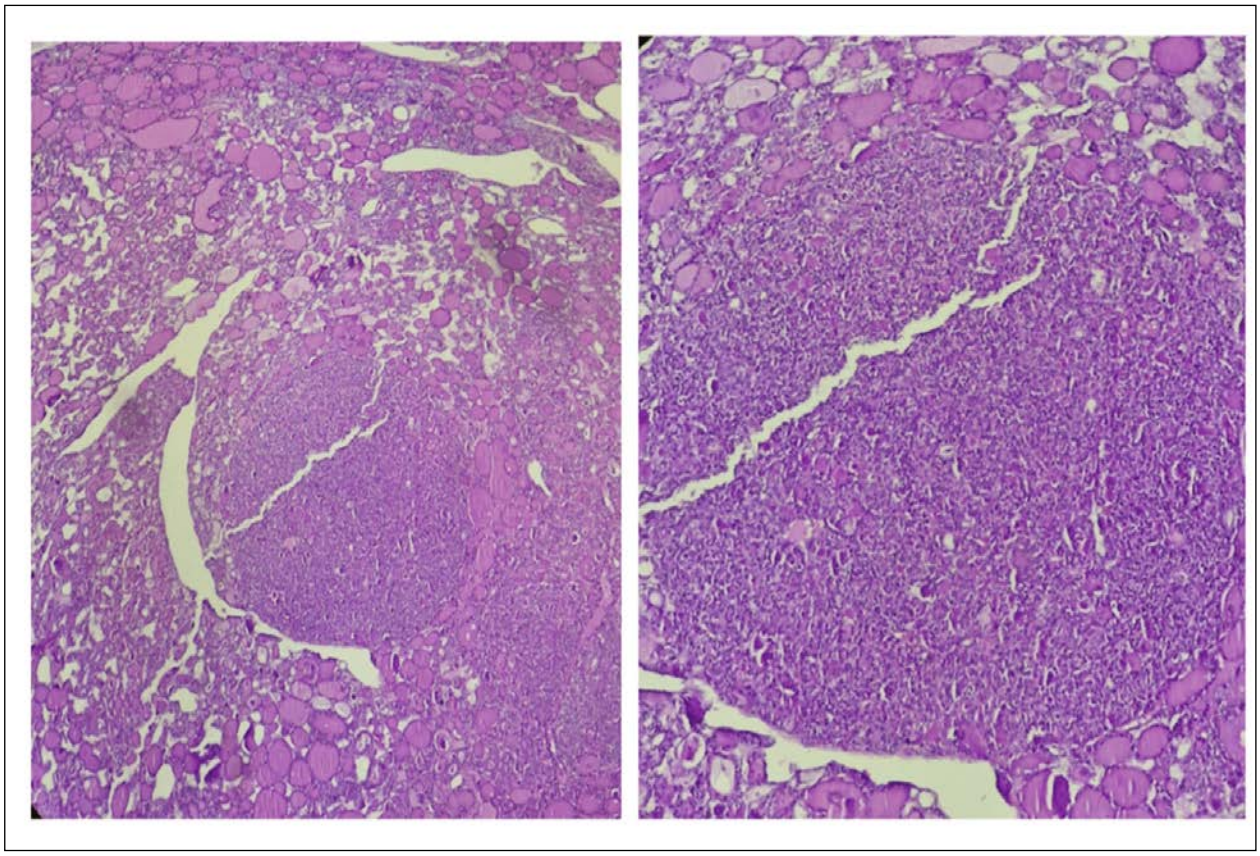

Figure 1: *Histological appearance of thyroid follicles lesion with abundant colloid and a single focus characterized by the formation of abnormal-looking, clustered thyroid follicular cells with an abnormal appearance and grouped together [6]*

Figure 2: *Benign multilocular complex cystic resembling thyroid tissue to the naked eye [6]*

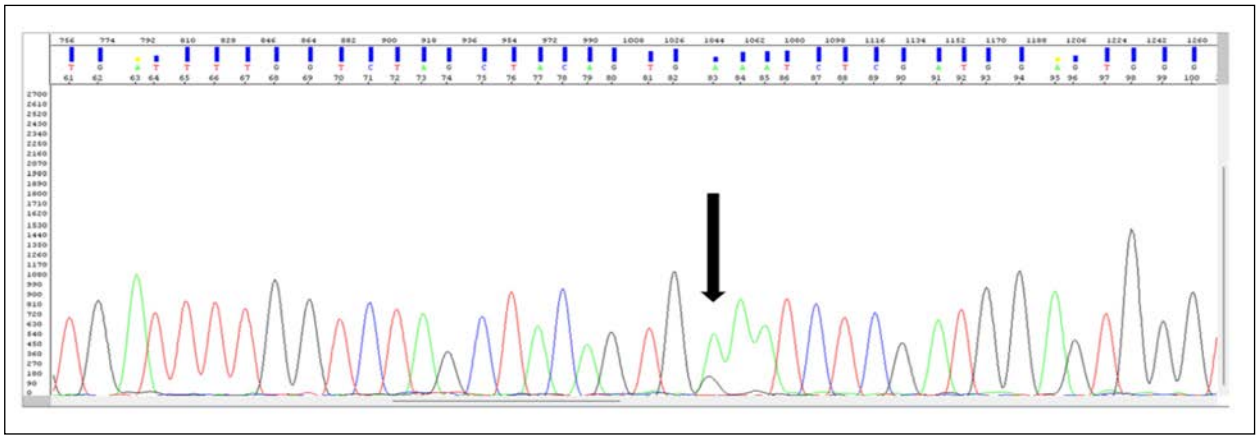

Figure 3: *Molecular study revealing the presence of the C.1801A>G p. K601E mutation on exon 15 of the BRAF gene [6]*

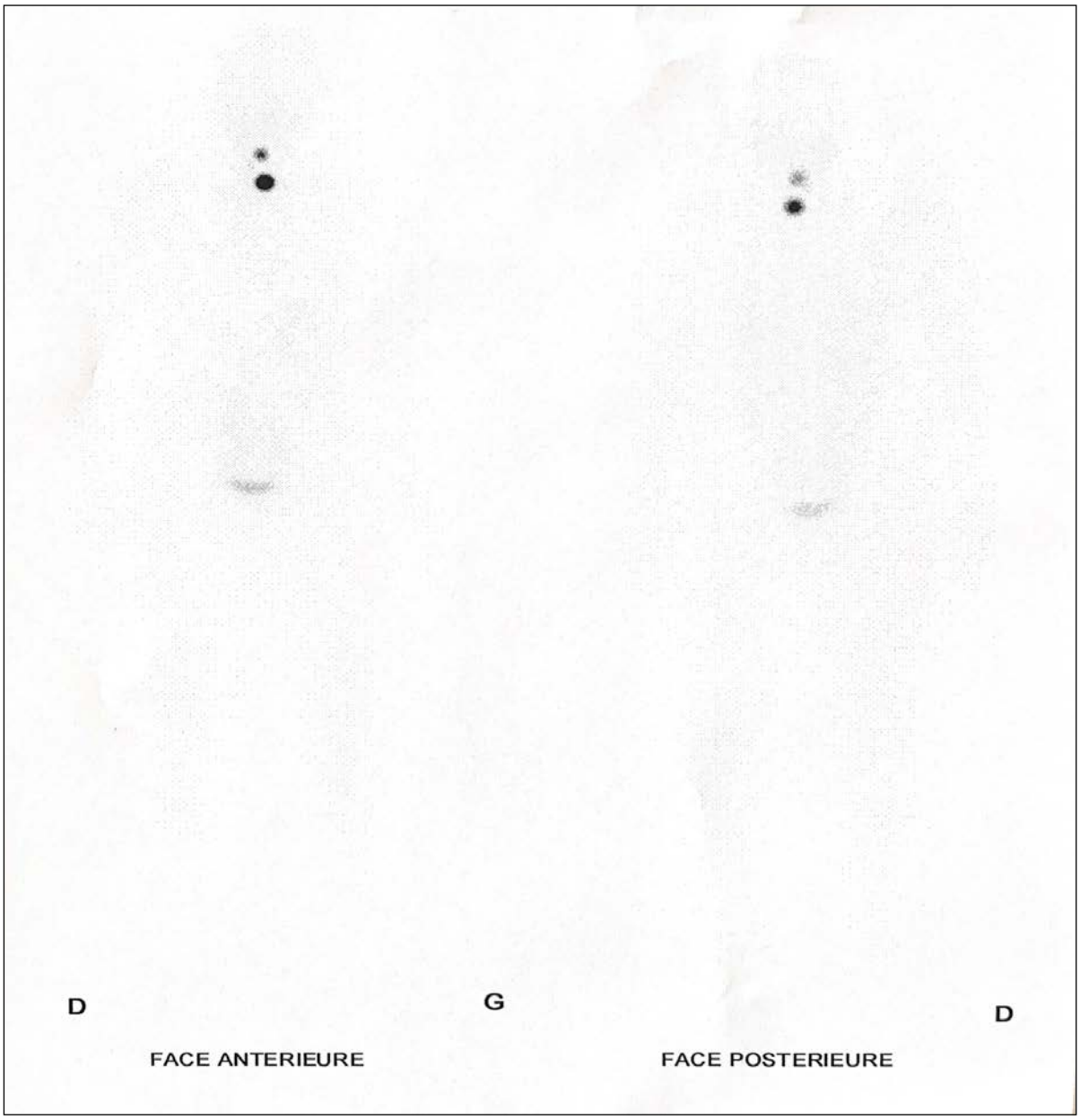

Figure 4: *Whole-body scan with iodine-131 showing two areas of iodine uptake in the thyroid bed with no other areas of pathological uptake elsewhere.*

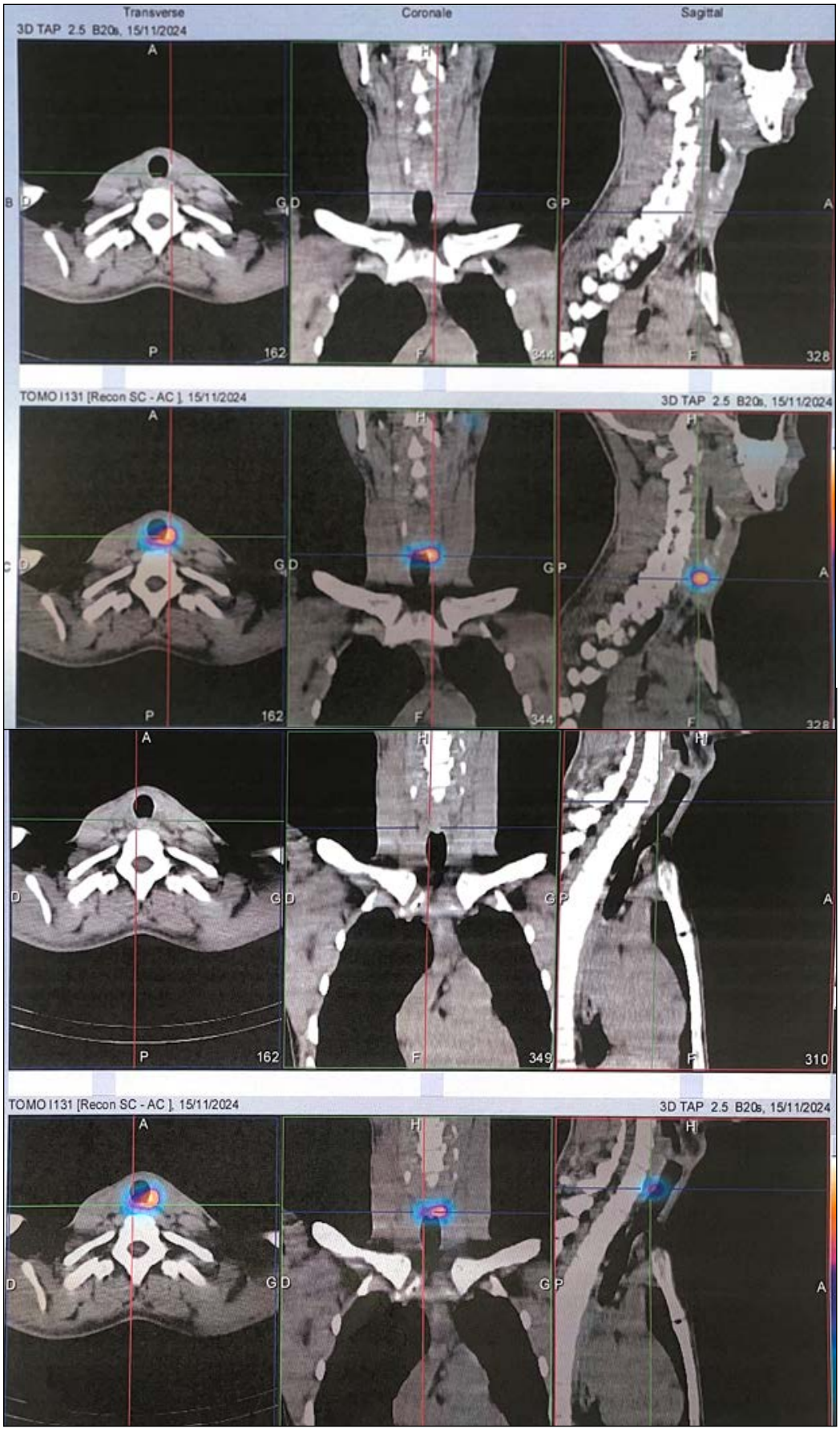

Figure 5a+b: *Cervico-mediastinal SPECT CT showing two areas of iodine uptake in the thyroid bed associated with thyroid remnants.*