A Case of Radiation-induced Differentiated Thyroid Cancer

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Swiss Journal of Radiology and Nuclear Medicine - www.sjoranm.com - Rosenweg 3 in CH-6340 Baar, Switzerland

Abstract

Introduction

The association between differentiated thyroid cancer and exposure to ionizing radiation has been well-known since the radioactive fallout of the 20th century [1]. Follow-up consultations after radiotherapy must address three major objectives: the assessment of oncological response, the evaluation of acute or late toxicity to ionizing radiation, and the screening for a second cancer [2]. Surveillance is especially indicated for cases with external irradiation such as patients with a history of cervical, upper mediastinal, craniospinal, or total body radiotherapy, in addition to internal contamination exposures due to nuclear accidents. This risk is limited to the development of differentiated thyroid cancer, namely papillary or follicular types [2]. In fact, the risk is highest for irradiation received before the age of five and decreases with age, becoming non-significant if irradiation takes place after 15 to 20 years of age [3].We report a case of radiation-induced papillary thyroid carcinoma in a 16-year-old adolescent, managed in the Nuclear Medicine Department at Hassan II-Fez University Hospital Center.

Keywords: *Ionizing radiation, differentiated thyroid cancer, radioiodine therapy*

[*]Corresponding author: Arnauld Muhoza - received: 06.12.2025 - peer reviewed, accepted and published: 31.12.2025

Introduction

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Observation

This is a 16-year-old female patient presenting with height and weight growth retardation for the past two years, with a medical history of posterior fossa medulloblastoma diagnosed and surgically treated at the age of 5 years. She underwent cranial and posterior fossa irradiation with 21 sessions totaling 55.8 Gy (end of irradiation 25th September 2013) and was subsequently declared cured under annual clinical and radiological surveillance. In 2024, she presented to the pediatric clinic with a WHO stage 3 cervical swelling of thyroid origin. Cervical palpation found a thyroid nodule associated with cervical adenopathy. Cervical ultrasound revealed a 25*23 mm nodule in the right thyroid lobe, classified EU-TIRADS 4, with suspicious adenopathy in lymph node chains IIa, III, and IV. The baseline diagnostic chest-abdomen-pelvis CT scan revealed pulmonary micronodules. Fine-needle aspiration was not performed due to the inaccessibility of the nodule. A total thyroidectomy with lymph node dissection was performed in August 2024, and the pathological examination of the thyroid specimen and

lymph node areas found a differentiated thyroid cancer classified as pT1bN1bM1 (Figure 1). The patient was subsequently referred to the nuclear medicine department for iratherapy. She received her first course of radioiodine therapy about 10 weeks after surgery with 50 mCi (1.85 GBq). The peri-radioiodine assessment in a withdrawal state showed: TSH 64.3 mUI/ml, thyroglobulin 110 ng/ml, negative anti-thyroglobulin antibodies. The whole-body scan indicated residual thyroid tissue with multiple pathological areas of uptake in the lungs (Figure 2), corresponding to nodules described on the initial CT. The remainder of the initial CT showed an empty thyroid bed with no cervical adenopathy. The second course of radioiodine therapy was administered with 50 mCi (1.85 GBq). The assessment on withdrawal showed: TSH 64.4 mUI/ml, thyroglobulin 40 ng/ml, anti-thyroglobulin antibodies 32.4 IU (negative). The whole-body I-131 scan showed slight residual thyroid tissue and regression of multiple pathological pulmonary uptake foci (Figure 3). The subsequent CT scan showed an empty thyroid bed with no cervical adenopathy and notable regression (>30%) of pulmonary nodules, most of which had become calcified. A third course of radioiodine therapy was administered at a dose of 100 mCi (3.7 GBq). The withdrawal assessment revealed: TSH 64.4 mUI/ml, thyroglobulin 5 ng/ml, anti-thyroglobulin antibodies 20 IU (negative). The whole-body scan showed complete resolution of pathological pulmonary uptakes (Figure 4). The CT scan revealed no pathological enhancement in the cervical compartment and calcified micronodules associated with an interstitial syndrome. The patient is currently declared cured based on clinical, biological, and morpho-functional criteria with annual follow-up of tumor markers under suppressive-dose L-Thyroxine, targeting a high-risk TSH goal for the first five years to mitigate recurrence risk.

Discussion

Differentiated thyroid cancer in children, whether apparently spontaneous or secondary to irradiation, is a rare entity. It is exceptional before the age of ten, and its incidence increases with age [3], [4]. During childhood, the thyroid gland remains the most sensitive organ to the carcinogenic effects of ionizing radiation for several reasons [1, 5]. External irradiation for the treatment of benign or malignant diseases during childhood increases the risk of developing thyroid tumors after a latency period of at least five years. Additional risk factors include the combination of irradiation and chemotherapy, particularly with alkylating agents at doses below 20 Gy, female sex, and younger age at cancer treatment onset. This increased risk persists throughout life and justifies continuous follow-up beyond five years [1], [2], [5].

The mechanisms by which ionizing radiation induces thyroid cancer are multiple and not yet fully understood [5]. Through stochastic effects, DNA damage and the induction of genetic instability promote the accumulation of lesions leading to the transformation of normal cells into cancerous ones [5]. Moreover, the higher rate of cell mitosis in children compared to adults predisposes them to an increased risk. It has also been noted that the radiation dose relative to thyroid gland weight in children plays a major role in determining the extent of damage. The suspicion of a radiation-induced cancer, as opposed to an apparently spontaneous one, relies mainly on epidemiological evidence: a correlation exists between childhood radiation doses exceeding 100 mSv, received at least five years prior to cancer onset, and genetic predisposition [4]. According to Misaoui et al., the risk of developing a thyroid tumor represents approximately 80% for ionizing radiation doses of 1 Gy absorbed by the thyroid during childhood [4]. In our patient, despite an exhaustive genetic evaluation showing no predisposition, a cervical irradiation dose of 55.8 Gy at the age of five explains this risk. The differential diagnosis includes familial forms of differentiated thyroid cancer found in 5–10% of children, mainly syndromic familial diseases such as Cowden disease, Gardner syndrome or familial adenomatous polyposis, and Werner syndrome [3]. The absence of clinical signs and negative genetic testing excluded these conditions in our case.

From a histopathological standpoint, radiation-induced and apparently spontaneous thyroid cancers share up to 80% of their features, most frequently of the classical type [5]. Aggressive histologic variants, such as the solid or diffuse sclerosing types, are more closely associated with younger age at onset than with radio-induced etiology [5]. The classic papillary subtype is the predominant form of thyroid cancer in children, accounting for 85–93% of cases, with a slow progression and limited spread. It usually occurs in older children and adolescents. Our patient presented with a classical papillary thyroid carcinoma consistent with findings in the literature. More aggressive variants, often seen in younger children, tend to present with more extensive disease at diagnosis [3].

Cervical lymph node metastases are frequent at diagnosis, with an incidence exceeding 75% in some pediatric series. Our patient had a nodal status of N1b. Lymphadenopathies are often palpable (23–74% of cases depending on the series) and must be distinguished from benign adeno-

pathies. Pulmonary metastases are more common in children than in adults, occurring in up to 25% of pediatric cases versus less than 5% in adults [3]. In our patient, pulmonary metastases were detected on whole-body post-therapy scans after the first treatment (M1 status). The advanced stage at diagnosis and management may be explained by a two-year delay in consultation.

The management of radiation-induced thyroid cancers is similar to that of apparently spontaneous differentiated thyroid cancers, depending on recurrence risk according to the 2025 ATA recommendations and the TNM staging system (UICC/AJCC revised 2017) [2], [6]. Radioiodine therapy is recommended at a dose of 1 mCi/kg, with therapeutic doses ranging between 1.85 and 3.7 GBq (50–100 mCi) [7]. Our patient received two treatments at 50 mCi and a third one at 100 mCi. However, thyroid cancers in younger children are often more extensive at diagnosis [3]. Close monitoring is imperative to prevent complications associated with radiation-induced thyroid cancer [5], and lifelong follow-up is required because of the risk of very late recurrences [7].

Despite favorable progress, our patient remains under lifelong clinical, biological, and imaging surveillance, including annual tumor marker evaluations under L-Thyroxine therapy at a dose of 2.4 µg/kg, with imaging as indicated. From a prognostic perspective, radiation-induced and apparently spontaneous thyroid cancers share a similar outcome, generally favorable in well-differentiated classical forms and less favorable in aggressive or poorly differentiated variants, provided that initial treatment is appropriate and follow-up is prolonged [5], [8]. Overall survival is excellent typically above 90% at 20 years with very low mortality for both sporadic and radiation-induced forms [9].

As for the risk of developing a second (or third, in our case) malignancy, Barrington de Gonzalez, in a study of 647'672 cancer patients over 12 years, found a lower risk in only 9% of cases [8]. The occurrence of a second cancer was more closely linked to lifestyle and genetic factors than to irradiation [8]. To minimize the risk of further radiation-induced cancers following irradiation, careful use of imaging follow-up and justified radiation dosing should help prevent the development of additional malignancies, particularly breast cancer and leukemia in our patient's context.

Conclusion

Systematic follow-up after irradiation beyond certain doses in childhood is essential to identify complications such as radiation-induced differentiated thyroid cancers. Even minimal exposure to ionizing radiation during childhood carries a significant risk for the thyroid. The prognosis of radiation-induced cancers in children remains favorable when managed early. Special attention should be given to children with a history of cervical, upper mediastinal, craniospinal, or total body radiotherapy.

Figures

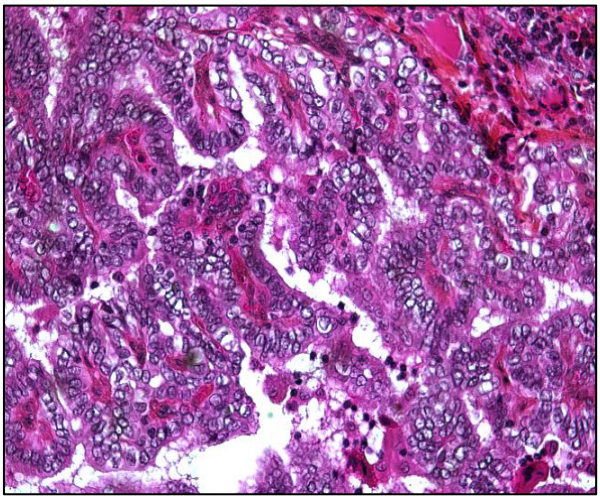

Figure 1(a): Histological examination from thyroid fragments and cervical lymph nodes revealed a tumoral proliferation arranged in papillary and vesicular structures, centered around fibrovascular cores, producing a classic ground-glass appearance

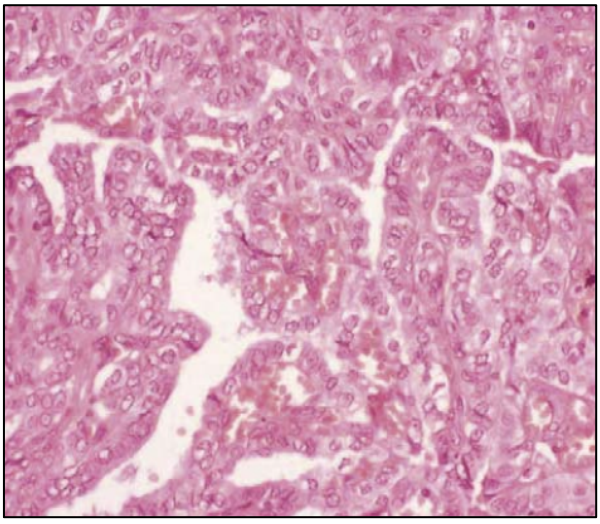

Figure 1(b): Histological examination from thyroid fragments and cervical lymph nodes revealed a tumoral proliferation arranged in papillary and vesicular structures, centered around fibrovascular cores, producing a classic ground-glass appearance

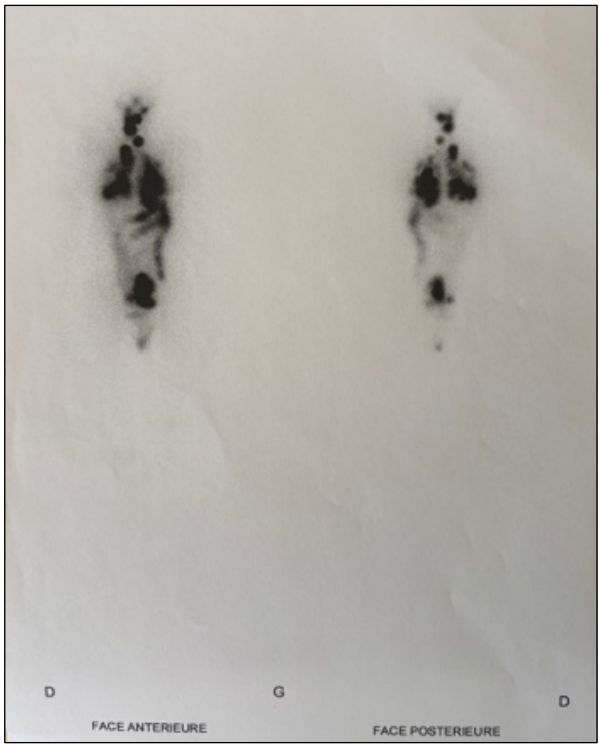

Figure 2: Post-first-treatment whole-body scan with iodine-131 demonstrated the presence of iodine-avid thyroid remnants, along with multiple sites of pathological uptake in the lungs corresponding to micro- and macronodular pulmonary lesions

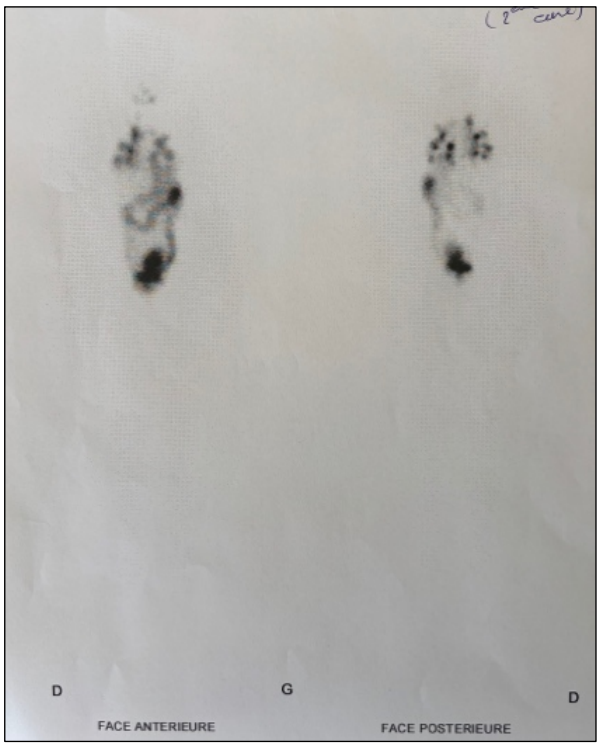

Figure 3: Post-second-treatment whole-body scan with iodine-131 revealed a small thyroid remnant and marked regression of abnormal uptake in both lung fields

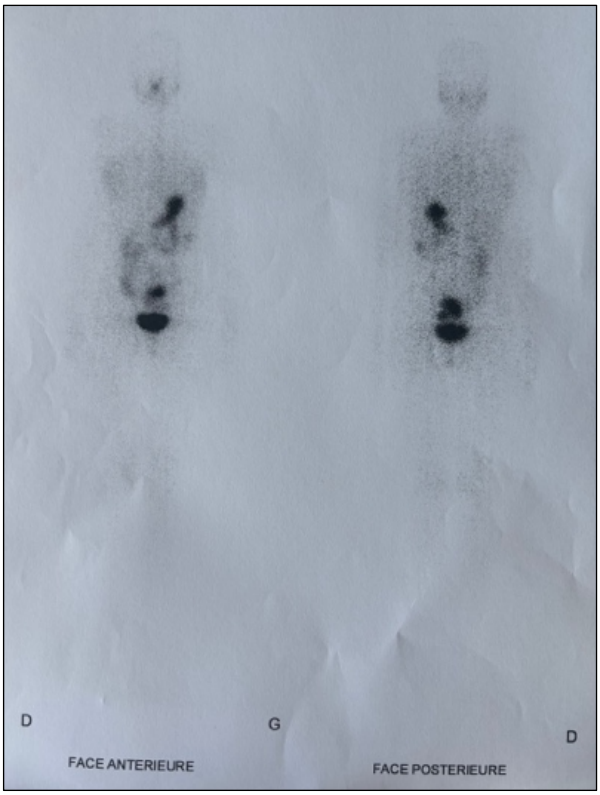

Figure 4: Post-third-treatment whole-body scan with iodine-131 showed complete resolution of the abnormal pulmonary uptake sites

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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.
Competing interests: No competing interests.
Funding: No funding was required for this study.

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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