Orbital Radioiodine Uptake on Scintigraphy in a Patient with Thyroid Cancer

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Established Facts

- Orbital radioiodine uptake is highly uncommon, and some conditions associated with this finding are metastases as well as false-positive results due to contamination, inflammation, etc.
- Cystic structures located in the bronchus, kidney, liver, or ovary are previously reported causes of false-positive results in scintigraphy.

Novel Insights

- To our knowledge, this is the first reported case of a conjunctival epithelial inclusion cyst associated with incidental radioiodine uptake in the orbital region.

Keywords

Papillary thyroid carcinoma · Scintigraphy · Orbital radioiodine uptake · Conjunctival inclusion cyst

Abstract

Background: Orbital radioiodine uptake in patients with thyroid cancer is very uncommon with only a few reported cases, most of them being metastasis. The accumulation of ¹³¹I in nonthyroidal tissues and body fluids can lead to false-positive results in scintigraphy, which are sometimes diffi-

cult to differentiate from true metastases. **Case Report:** A post-therapy ¹³¹I whole-body (WBI) scintigraphy in an asymptomatic 57-year-old female with papillary thyroid carcinoma (PTC) previously treated with total thyroidectomy and 6 ablative radioiodine doses showed a focal uptake in the right eyeball region. The lesion, placed in the orbital space, was surgically removed, and histology revealed a conjunctival inclusion cyst. **Discussion:** Ocular and orbital metastases from thyroid cancer, as well as some non-neoplastic disorders or contamination, are possible causes for ¹³¹I up-

take in the orbital region in scintigraphy. Conjunctival inclusion cyst is a condition associated with incidental ^{131}I uptake that had not been reported before and should be ruled out as a non-metastatic cause of orbital radioiodine uptake in patients with PTC.

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Introduction

Differentiated thyroid cancer is one of the most prevalent solid tumor types with a rising incidence, and papillary thyroid carcinoma (PTC) represents the most frequent variant [1]. Due to the capacity of metastatic thyroid cells to take up iodine from blood, distant metastases from PTC, which are relatively uncommon, can sometimes be detected during a post-therapy whole-body iodine scan (WBI) performed after treatment with radioactive iodine [2]. While, globally, the most common metastatic sites are cervical lymph nodes, distant metastases typically involve lungs, bones, and, less frequently, the brain [3]. Only in rare cases, patients may present metastases in unusual locations such as the choroidal, uveal or orbital region [4, 5].

Since both physiological and pathological accumulation of ^{131}I in nonthyroidal tissues and body fluids can lead to unexpected radioiodine uptake in WBI, these findings in patients with PTC might also be misleadingly attributed to the presence of true distant metastases [2].

Case Report

We report the case of a 62-year-old female with a history of PTC (follicular variant) treated with total thyroidectomy in 1998. She received six radioiodine doses (cumulative dose of 26.83 GBq; 725 mCi), with biochemical progressive responses following the first five doses, starting from a stimulated thyroglobulin value of 30.4 ng/mL in May 1999 (1 month after levothyroxine withdrawal) and a basal level of 1.16 ng/mL in September 1999 (suppressed by levothyroxine therapy). WBI scans after receiving the first four ^{131}I doses showed no abnormal uptake outside the cervical region. However, in 2007, after the fifth adjuvant dose, a post-therapy scintigraphy showed two small areas of nodular radioiodine uptake in the skull (previous stimulated thyroglobulin 3.13 ng/mL). Afterwards, the patient underwent regular biochemical assessments, cervical ultrasounds, fine-needle aspirations when indicated, and two 18-F-fluorodeoxyglucose positron emission tomography integrated with computed tomography (18F-FDG PET/CT) in 2010 and 2013, respectively. Both 18F-FDG PET/CT were performed after recombinant TSH administration and revealed increased 18F-FDG uptake in two lymph nodes in the right lateral neck that were reported as nonpathologic and stable in size and

intensity. Fine-needle aspirations of the right lymph nodes were not conclusive, and no evidence of metastatic disease could be cytologically demonstrated.

Although basal suppressed thyroglobulin levels remained always very low or undetectable after 2007 (usually below 0.2 ng/mL), consecutive recombinant TSH-stimulated thyroglobulin levels, after reaching a minimum in 2008 (0.82 ng/mL), displayed a slow but constant increasing trend that reached a maximum of 4 ng/mL in November 2014. Therefore, in January 2015, based on the elevated thyroglobulin levels and considering the findings of the previous imaging tests, the patient received a sixth adjuvant radioiodine dose of 5.55 GBq (150 mCi) after stimulation with recombinant TSH (thyroglobulin 1.03 ng/mL). After 96 h, a post-treatment WBI scintigraphy showed high focal uptake in the right facial region as well as physiological tracer distribution and a focus of uptake in the left hand (Fig. 1a). Additional static images of abdominopelvic and head regions were taken, confirming that the left hand uptake was a contamination and ruling it out in the facial region. The head single-photon emission computed tomography/computed tomography (SPECT/CT) image showed that the uptake was located in the right orbital region (Fig. 1b). The patient did not report any visual symptom. All previous post-therapy WBI scans were thoroughly revised, and no uptake was found in the orbit in any of them. The orbital focus was reported as an incidental finding in the scintigraphy. A magnetic resonance imaging (MRI) was performed, showing a well-defined $14 \times 7 \times 10$ mm lesion in the right postseptal orbital space. Axial T2-weighted fat-saturated image showed heterogeneous signal, predominantly hypointense, with central hyperintense foci (Fig. 2a). MRI after gadolinium contrast administration revealed homogeneous enhancement (Fig. 2b). This orbital lesion was already present in the CT images of the two 18F-FDG PET/CT performed previously.

The intraorbital lesion was surgically removed, and the histopathological report described a cystic lesion, lined by pseudostratified columnar epithelium with goblet cells. These findings were consistent with the diagnosis of a conjunctival epithelial inclusion cyst. To our knowledge, this is the first reported case describing an incidental radioiodine uptake produced by a conjunctival inclusion cyst.

Discussion

Orbital uptake on a ^{131}I scan is an exceptional finding. Some cases of choroidal, uveal, or orbital metastases from differentiated thyroid carcinoma have been reported [4, 5]. In contrast to our patient, most of these patients presented symptoms such as decreased visual acuity, blurred vision, eye pain, proptosis or diplopia [4, 5]. Interestingly, other non-neoplastic conditions can lead to false-positive results. ^{131}I uptake has been reported in cystic structures such as bronchogenic, renal, hepatic, ovarian, sebaceous, or epithelial cysts [6, 7]. In these cases, the mechanism seems to be the entry of radioiodine via passive diffusion and retention inside the cyst. However, the expression of

Fig. 1. **a** WBI scintigraphy anterior view showing high focal uptake in the right facial region as well as physiological tracer distribution and a focus of uptake in the left hand. **b** SPECT/CT image showing localized uptake in the right orbital region.

Fig. 2. MRI showing a lesion of $14 \times 7 \times 10$ mm with well-defined margins located in the right postseptal orbital space. **a** Axial T2-weighted fat-saturated image showing heterogeneous signal, predominantly hypointense, with central hyperintense foci (arrow). **b** Image after gadolinium contrast administration revealing homogeneous enhancement.

the sodium-iodine symporter in the cyst wall has also been proposed as a possible explanation, since it has been reported in extrathyroidal tissues, including ocular structures such as the lacrimal glands, choroid plexus, and ciliary body of the eye [7]. Inflammatory conditions such as uveitis or dacryocystitis may rarely result in ^{131}I uptake on a scintigraphy [8]. The higher incidence of lacrimal drainage system obstruction associated with high cumulative doses of ^{131}I therapy for thyroid carcinoma that has been described is able to boost the development of a dacryocystitis [9]. Moreover, contamination by bodily secretions such as tears, saliva, or sweat where ^{131}I can be excreted are other causes of false-positive results [7]. In this context, the accumulation of radioiodine in tears retained behind an artificial eye could explain the incidental uptake in the orbital region demonstrated in patients with ocular prosthesis [8, 10].

Using a parallel approach, it is also possible that in our case, the cyst, once formed in the right medial orbital angle, obstructed the normal aqueous humor drainage through the trabecular meshwork into Schlemm's canal, prolonging radioiodine retention inside the anterior and posterior chambers and enhancing the orbital uptake on the WBI scan. In fact, as mentioned above, the presence of sodium-iodine symporter expression has been reported in the ciliary body of the eye [7]; therefore, small amounts of radioiodine could be excreted in the aqueous humor and reach high concentrations in case of being retained.

Although the true etiology of the increased uptake in the skull found in the fifth scintigraphy is unknown, there are two possible explanations: bone metastases successfully treated with ^{131}I therapy or a false-positive result caused by contamination.

Conclusion

The presence of nonmetastatic lesions, especially in the absence of associated symptoms, should be ruled out in patients with differentiated thyroid cancer who show radioiodine uptake in the orbital region. Intraorbital conjunctival epithelial inclusion cysts had never been reported associated with incidental orbital radioiodine uptake in patients with thyroid cancer, but according to our experience, they do not imply a poorer prognosis and can be successfully resected by surgery.

Statement of Ethics

The subject in the case report gave her informed consent. There was no need for institutional review board approval as it is only a case report with a review and did not have a study protocol.

Disclosure Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Author Contributions

R.M.G. drafted the paper and conducted the literature review. C.E., C.U., E.R. and M.S. provided images and relevant information about the case. B.L. suggested to report this case, revised the manuscript making the required corrections, and is the endocrinologist who currently follows the patient.

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