Iodine-131 Therapy and Lacrimal Drainage System Toxicity: Nasal Localization Studies Using Whole Body Nuclear Scintigraphy and SPECT-CT

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Purpose: The objective of this study was to evaluate the influence of dose on nasal localization of radioactive iodine-131 (I-131) following therapy for differentiated thyroid carcinomas.

Methods: Retrospective evaluation of all patients who underwent post-therapy I-131 whole body scintigraphy and single photon emission computed tomography was performed. Patients were divided into 2 groups; group A were treated with 100 millicurie (mCi) and group B with ≥150 mCi. Databases were reviewed for demographics, diagnosis, and administered dosage of I-131. Whole body scintigraphy images were retrieved and nasal uptake was analyzed and classified as nil to trace, low, moderate, and high uptake and corresponding single photon emission CTs were analyzed for radioactive nasal activity.

Results: A total of 100 patients were studied, 50 in each of the groups. The M:F ratio was 1.1:1 (27:23) in group A and 1.5:1 (30:20) in group B. The mean age was 43.12 years and 54.6 years in groups A and B, respectively. Papillary carcinoma of the thyroid was the most common type accounting for 82% (41/50) of patients in group A and 62% (31/50) in group B. Imaging studies revealed nil to trace nasal activity in 80% (40/50) in group A as compared with 56% (28/50) in group B. None of the patients in group A showed high nasal uptake, whereas 4% (2/50) in group B demonstrated such high activity.

Conclusion: Intranasal localization of radioactive I-131 was significant in patients receiving a dose of ≥150 mCi. Intranasal localization may partly explain toxicity to nasolacrimal duct and may be a risk factor for subsequent development of nasolacrimal duct obstructions.

(*Ophthal Plast Reconstr Surg* 2015;XX:00–00)

Iodine-131 (I-131) therapy is a well established modality of managing variety of thyroid disorders like Graves disease, differential thyroid carcinomas (DTC) and metastatic disease.[1–10] The incidence of thyroid carcinomas is on the rise and DTC's are the most common of them and include papillary and follicular carcinoma.[1–5] The physical half life of I-131 is 8 days and emits beta (β) rays that are used for treatment and gamma (γ) rays which are used for diagnosis. The dose if I-131 for treatment of DTC and metastasis usually ranges from 75 mCi to 250 mCi.[1–5] Following oral administration of I-131, iodide uptake happens across the follicular cells of the thyroid or neoplastic cells through a sodium-iodine symporter (NIS) active transport.[6–8] The NIS protein has been demonstrated not only in thyroid tissues but also in gastric mucosa, salivary glands, breast, thymus, and lacrimal drainage system. In addition, liver and bladder show activity on whole body scintigraphy (WBS) because they are routes of excretion. However, abnormal tissues like ectopic thyroid gland, inflamed and infected tissues, benign and malignant tumors and effusions of serous cavities show false-positive I-131 uptake.[9]

The early side effects of I-131 therapy include nausea, acute sialadenitis, xerostomia, epistaxis, thyroiditis, and stomatitis.[10] The long-term side effects include chronic sialadenitis, xerostomia, xerophthalmia, chronic conjunctivitis, salivary and nasolacrimal duct (NLD) obstructions, infertility, pulmonary fibrosis, bone marrow aplasia, and rarely second primary malignancies.[10] Nasolacrimal duct obstructions (NLDO) and epiphora following I-131 therapy is sparsely documented in literature and a direct relationship has not been conclusively proven.[11–19] The frequency of NLDO is reported to range from 3.4% to 11% following the therapy.[14,17–19] The current study specifically examined the nasal tissue localization of I-131 using WBS and single photon emission computed tomography (SPECT) imaging in an effort to possibly explain the NLD toxicity.

METHODS

Institutional review board approval was obtained prior to conduct of the study. Retrospective evaluation was performed on all patients with DTCs who underwent radioactive I-131 residual ablation therapy from 2011 to 2015 for residual disease following thyroidectomy. All patients were administered oral sodium iodide I-131 solution (Jubilant Draximage, Kirkland, Canada). Patients who underwent whole body I-131 scintigraphy and single photon emission computed tomography (SPECT-CT) at 1 week following oral administration were included in the study. Patients were divided into 2 groups based on the dosage they received; group A were treated with 100 millicurie (mCi) and group B with ≥150 mCi. Databases were reviewed for demographics, diagnosis, and administered dosage of I-131. Whole body I-131 scintigraphy images were retrieved and nasal uptake was analyzed and classified as nil, low, moderate, and high uptake based on the software color coding (Esoft Syngo, Siemens, Erlangen, Germany). The corresponding SPECT-CT's were analyzed for radioactive nasal activity.

RESULTS

A total of 100 patients were recruited, 50 in each of the groups. The M:F ratio was 1.1:1 (27:23) in group A and 1.5:1 (30:20) in group

Accepted for publication October 21, 2015.

Dr. Ali receives royalties from Springer for his textbook "Principles and Practice of Lacrimal Surgery". The other authors have no financial or conflicts of interest to disclose.

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DOI: 10.1097/IOP.0000000000000603

B. The mean age was 43.12 years (range: 21–87 years) and 54.6 years (range: 25–77 years) in groups A and B, respectively. Papillary carcinoma of the thyroid was the most common type accounting for 82% (41/50) of patients in group A and 62% (31/50) in group B. The remaining cases in both the groups had follicular carcinoma of the thyroid. All the patients in group A received a dose of 100 mCi, whereas the mean dose in group B was 174 mCi (median: 150 mCi, range: 150–250 mCi). Imaging studies revealed nil to trace nasal uptake in 80% (40/50) in group A as compared with 56% (28/50) in group B (Fig. 1A, B). Group A patients showed low nasal uptake in 14% (7/50) and moderate in 6% (3/50). There were no high uptake patients in group A. Group B patients showed low nasal uptake in 32% (16/50), moderate in 8% (4/50), and high uptake in 4% (2/50). Figures 1 and 2 reflect the varying degrees of uptake recorded by I-131 WBS. The corresponding low to high uptakes were confirmed on SPECT-CT activities (Fig. 3). The uptake was seen at the tips, lateral walls as well as nasal cavity. Figure 4 depicts bar diagram summarizing the results.

DISCUSSION

The current imaging study performed detailed image evaluation and classification of nasal uptake of radioactive I-131 in patients of DTCs. Intranasal localization of radioactive I-131 was significant in patients receiving a dose of ≥150 mCi. High intranasal radioactivity was noted on WBS and SPECT-CT only in patients with doses ≥150 mCi. High levels of uptake by the nasal tissues can be a predictor for toxicity to the lacrimal drainage system and possibly subsequent development of NLD obstructions.

Following I-131 therapy, imaging is performed at around 1 week using the I-131 whole body scanning to confirm the radioactive dye targeting of tissues of thyroid origin, detection and targeting of residual tumor tissues or metastasis. Although I-131 WBS is a good imaging modality, its anatomical delineation is poor and physiological uptakes can make image interpretation a little difficult.[20] However, reliability of I-131 WBS has significantly improved when combined with SPECT-CT. The combination of both the modalities lead to better staging of the cancer, accurate anatomical localization of the scintigraphic lesions, and better delineation of physiological and pathological uptakes.[9,20,21] This study utilized both I-131 WBS and SPECT-CT image for studying the intranasal localization of radioiodine.

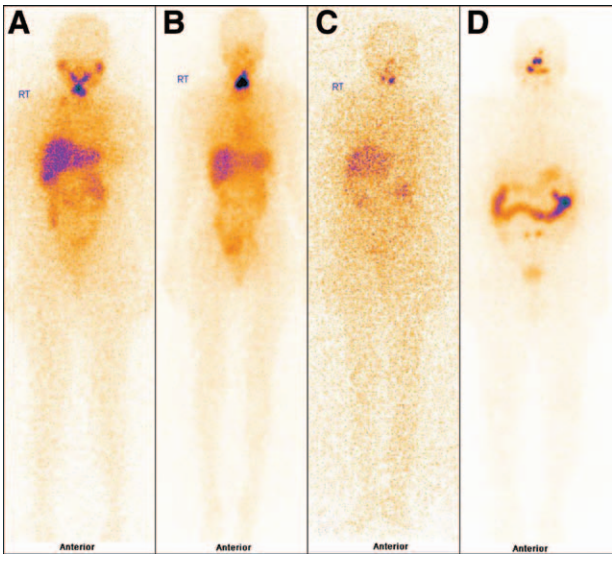

FIG. 1. Whole body I-131 planar scintigraphy: anterior views showing examples of nil to trace nasal uptake (**A**), low uptake (**B**), moderate uptake (**C**), and high nasal uptake (**D**).

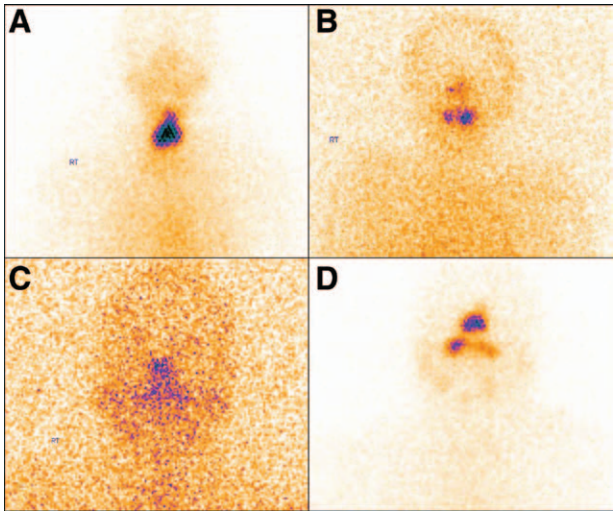

FIG. 2. Planar I-131 scintigraphy, head and neck windows: anterior views showing examples of nil to trace uptake (**A**), low uptake (**B**), moderate uptake (**C**), and high uptake (**D**).

I-131 toxicity to the lacrimal drainage system have been postulated to be secondary to the presence of NIS protein in the stratified columnar epithelium of the lacrimal sac and NLDs, as demonstrated in well-designed histological studies. Following I-131 therapy, the epithelial cells concentrate the radioiodine within them leading to radiation toxicity, inflammation, fibrosis, and obstructions of the lacrimal lumens. Immunohistochemical studies revealed absence of the NIS protein in the lacrimal duct epithelial cells after the effects of I-131 therapy, which give more evidence to the possible direct relationship between NIS protein and NLDO. Most of the case reports published has shown that NLDO was more common in patients who were treated with a I-131 dose greater than 150 mCi.[14,16] However, doses less than 150 mCi (as low as 100 mCi) have also been reported to cause lacrimal dysfunction.[11,14,15] The current imaging study also found that moderate to high nasal localization of radioiodine was predominantly noticed in patients who received ≥150 mCi.

Atypical uptake of radioactive iodine has been demonstrated in cases of dacryocystitis and after routine I-131 therapy. Brockmann et al.[18] reported a 54-year-old lady who was treated with a cumulative dose of 700 mCi for papillary carcinoma of thyroid with metastasis. Bilateral epiphora was documented 6 months after the therapy. Routine WBS scan after 1 year showed marked tracer accumulation bilaterally in the region of medial orbits. Dacryocystography revealed bilateral NLD obstructions and the high activity disappeared following dacryocystorhinostomy. Shepler et al.[17] reported a 50-year-old lady with epiphora of 5 years duration that started following I-131 therapy. Thyrogen scan showed a focus uptake near the inner canthus which was initially thought to be a metastasis. Irrigation and probing confirmed a diagnosis of right NLD obstruction. The focus uptake disappeared following a dacryocystorhinostomy. Bakheet et al.[22] studied radioactivity in the tears of a patient following a low dose of 15 mCi of I-123 and observed that detectable amounts of radioactive material (0.01% in 4 hours) was secreted in first 4 hours after ingestion. These anecdotal reports along with evidence of nasal localization from the current study and the presence of NIS proteins in the stratified columnar epithelium points toward a significant possibility of

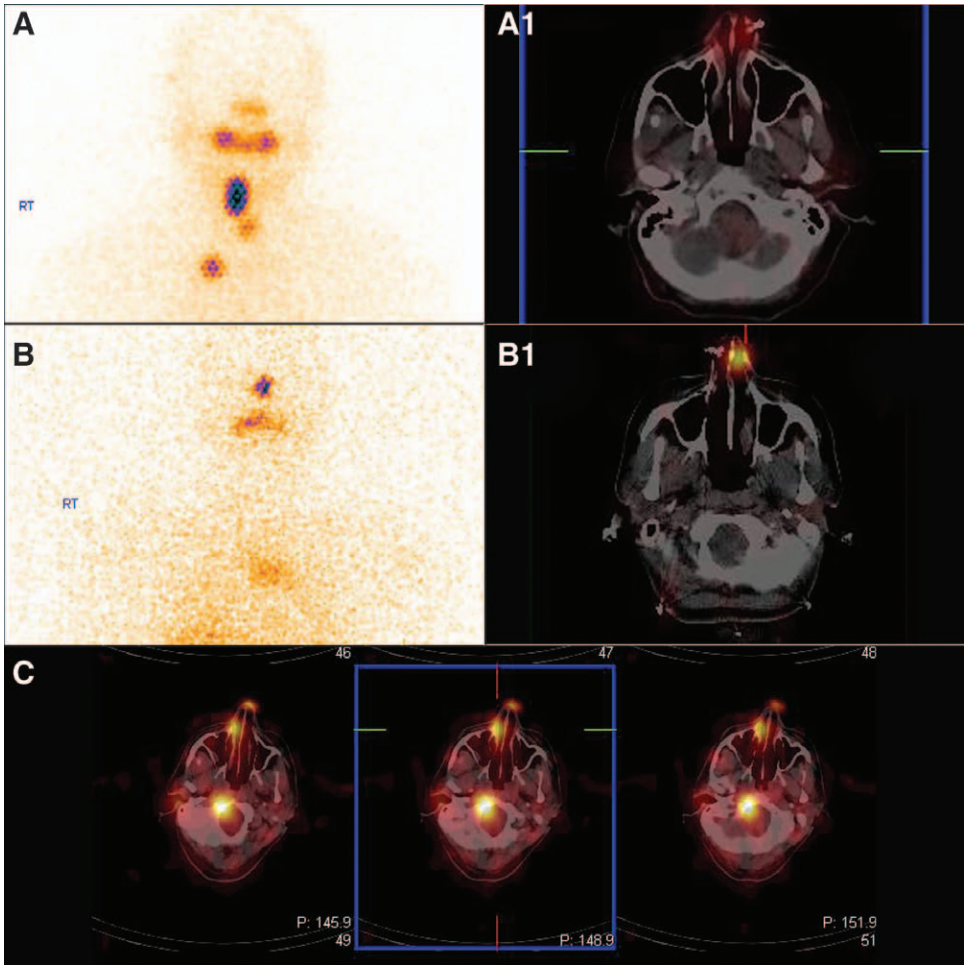

FIG. 3. I-131 SPECT-CT: **A**, 60-year-old female patient of papillary carcinoma, post administration of 100 millicurie of I-131. Note the low uptake on head and neck window of planar I-131 scintigraphy (**A**). Note the low, diffuse nasal uptake on axial cut section of SPECT-CT (**A1**). **B**, 29-year-old female patient of follicular carcinoma, postadministration of 150 millicurie of I-131. Note the moderate uptake on the head and neck window of planar I-131 scintigraphy (**B**). Note the moderately intense nasal uptake on axial cut section of SPECT-CT (**B1**). **C**, 60-year-old male patient of papillary carcinoma, postadministration of 150 millicurie of I-131. SPECT-CT, serial axial cuts showing high uptake of the nasal tip, septum and right nasal cavity and lateral walls (**C**). SPECT-CT, single photon emission computed tomography.

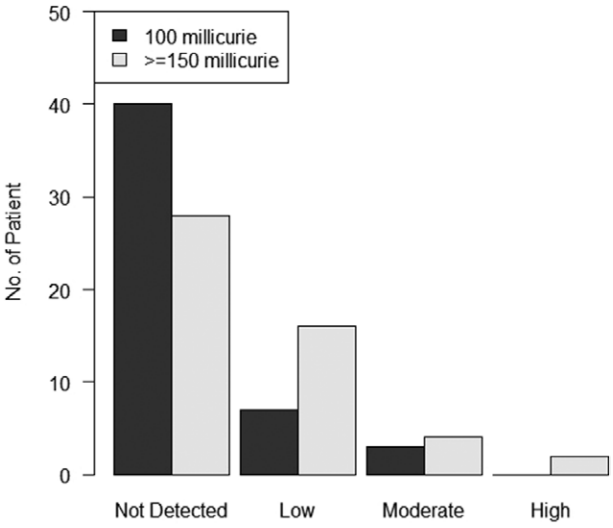

FIG. 4. Summary of the data results.

radio toxicity to the lacrimal drainage system from I-131 administration. The current evidence merits screening of all patients (pre- and post-I-131therapy), specifically those who receive a dose of more than 150 mCi.

The limitations of the current study are exclusion of few patients who require additional I-131 therapies for suboptimal thyroid ablation and hence may have more cumulative radio toxicity to the nasal tissues. In addition, this study looked only at the radiological features of nasal I-131 concentrations without clinical correlations.

In conclusion, intranasal localization of radioactive I-131 may partly explain toxicity to NLD and may be a risk factor for subsequent development of NLDO. Further studies corroborating intranasal uptakes with clinical symptoms and signs of lacrimal drainage toxicity are required to validate the findings of this study.

ACKNOWLEDGMENTS

The authors wish to acknowledge the help of Ms. Chinmayi Mungara during data collection and Mr. SBN Chary for help with photographs.

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