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Mammary radioiodine accumulation due to functional sodium iodide symporter expression in a benign fibroadenoma ☆

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Abstract

The sodium iodide symporter (NIS) has been characterized to mediate the active transport of iodide not only in the thyroid gland but also in various non-thyroidal tissues, including lactating mammary gland and the majority of breast cancers, thereby offering the possibility of diagnostic and therapeutic radioiodine application in breast cancer. In this report, we present a 57-year-old patient with multifocal papillary thyroid carcinoma, who showed focal radioiodine accumulation in a lesion in the right breast on a posttherapy ^{131}I scan following radioiodine therapy. CT and MR-mammography showed a focal solid lesion in the right breast suggestive of a fibroadenoma, which was confirmed by histological examination. Immunostaining of paraffin-embedded tumor tissue sections using a human NIS antibody demonstrated NIS-specific immunoreactivity confined to epithelial cells of mammary ducts. In conclusion, in a thyroid cancer patient we identified a benign fibroadenoma of the breast expressing high levels of functionally active NIS protein as underlying cause of focal mammary radioiodine accumulation on a posttherapy ^{131}I scan. These data show for the first time that functional NIS expression is not restricted to lactating mammary gland and malignant breast tissue, but can also be detected in benign breast lesions, such as fibroadenomata of the breast.

Keywords: Sodium iodide symporter; Breast; Radioiodine accumulation; Radioiodine therapy; Fibroadenoma

As an intrinsic plasma membrane glycoprotein, the sodium iodide symporter (NIS) mediates the active transport of iodide in the thyroid gland as well as a number of non-thyroidal tissues, including stomach, salivary gland, and particularly lactating mammary gland [1–3]. NIS-mediated iodide accumulation in the thyroid gland is not only the first and rate-limiting step in the process of thyroid hormone synthesis, but also allows imaging as well as effective therapy of differentiated thyroid carcinomas and their metastases by administration of radioiodine, thereby improving the prognosis and treatment of thyroid cancer significantly [1,4,5]. In lactating mammary gland iodide is actively transported and secreted into the milk in order to supply iodide to the infant for the biosynthesis of thyroid hormones, which are essential for the development of the nervous system, skeletal muscle, and lung [1]. In 2000 Tazebay et al. demonstrated NIS protein expression in mammary gland (mgNIS) and showed that it is the NIS protein that catalyzes iodide accumulation in lactating mammary gland [3]. In normal mammary tissue NIS is present exclusively during gestation and lactation, in contrast to the constitutive NIS expression in the thyroid gland, suggesting that hormones involved in active lactation stimulate NIS expression and/or its functional activity. Further *in vitro* and *in vivo* studies confirmed that lactogenic hormones, such as estrogen, prolactin, oxytocin, insulin as well as cortisol, are able to stimulate functional NIS expression in mammary tissue [3,6–10]. Moreover, besides

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NIS expression in lactating breast tissue, NIS expression has also been demonstrated in the majority of breast cancers on RNA and/or protein level by different investigators, indicating that NIS is frequently upregulated during malignant transformation in breast tissue [3,11,12]. These observations suggest that NIS expression in mammary carcinoma may offer the possibility of radioiodine application in the diagnosis as well as treatment of breast cancer.

In this report, we present a patient with multifocal papillary thyroid carcinoma, who showed focal radioiodine accumulation in the right breast region on a posttherapy ^{131}I scan following total thyroidectomy and radioiodine ablation of the thyroid remnant. Further investigation revealed a focal solid lesion in the right breast of the patient, which was biopsied and diagnosed as benign fibroadenoma of the breast expressing high levels of functionally active NIS protein detected by immunohistochemical analysis.

Imaging studies and case presentation

Imaging studies

Gamma camera imaging

Diagnostic whole-body ^{131}I scans were performed 48 h following oral administration of 370 MBq ^{131}I under endogenous TSH stimulation (TSH > 20 μU/ml). Posttherapeutic scans were performed four days after application of the therapeutic ^{131}I dose. The therapeutic ^{131}I dose was given seven days following the diagnostic ^{131}I application, to limit possible stunning effects.

Gamma camera imaging was performed using a gamma camera with a large field of view in ventral and dorsal orientation using a high energy collimator, which was especially optimized for ^{131}I applications. The localization of the breast lesion was further investigated using single photon emission computed tomography (SPECT), carried out on a Siemens ECAT gamma camera system directly after the posttherapeutic scan. Image reconstruction was performed using a standard filtered-back projection algorithm.

Conventional mammography

Conventional mammography was carried out with a dedicated digital mammography system (Mammomat 3000, Optima, Siemens, Germany).

CT scan of the thoracic region

A venous contrast enhanced CT scan (16 slice Somatom CT scanner, Siemens, Erlangen, Germany) of the thoracic region was performed using standard CT parameters. Contrast medium was applied at standard dose. CT images were fused with the SPECT images of the thoracic region utilizing the HERMES image fusion software tool.

MRI of the breasts

MRI of the breasts was performed utilizing a dynamic, contrast enhanced MR-mammography in flash 3D technique. Contrast medium was applied in standard dose.

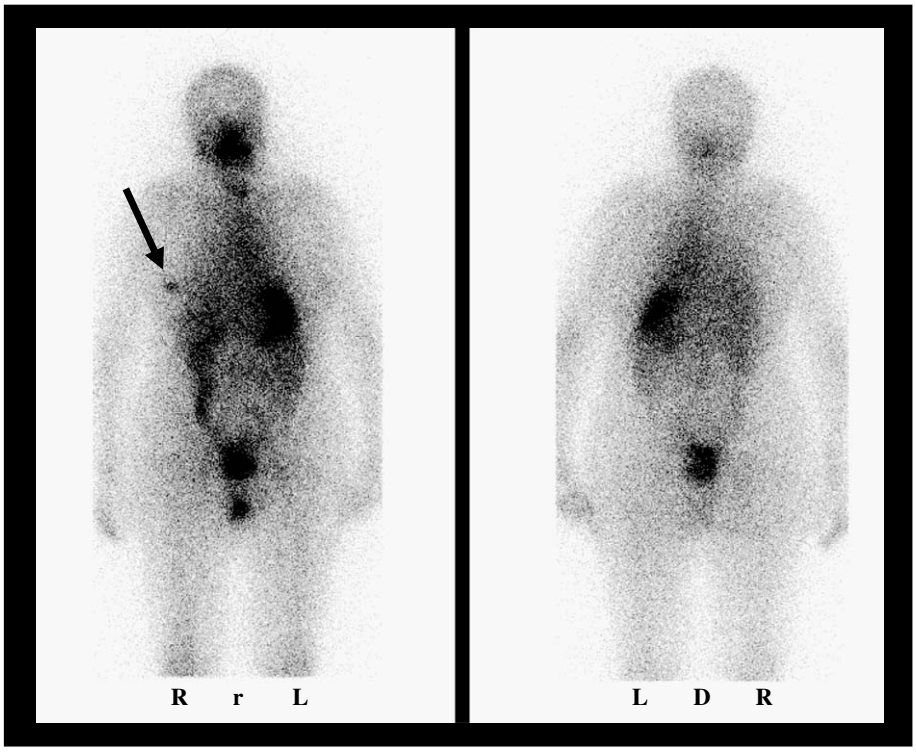

Fig. 1. Posttherapeutic ^{131}I whole body scan. The posttherapeutic ^{131}I whole body scan, performed four days after a second course of radioiodine treatment, showed mild iodine uptake in the former thyroid bed as well as focal dystopic radioiodine uptake in the region of the right breast (arrow).