Detection of Solitary Axillary Lymph Node Metastases from Hürthle Cell Carcinoma of the Thyroid on ^{18}F -FDG PET/CT

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Abstract

Thyroid carcinoma is the most common neoplasm of endocrine malignancies. Differentiated thyroid carcinoma (DTC) constitutes 90% of the thyroid carcinomas, rest being medullary thyroid carcinoma (MTC), and anaplastic thyroid carcinoma (ATC). Distant metastases occur in up to 10% of patients with DTC. Metastases to axillary lymph nodes (ALN) are very rare. As per literature, only 25 cases have been reported. We report an unusual case of 47-year-old male with Hürthle cell carcinoma of the thyroid presenting with a solitary axillary lymph node metastasis 17 years after thyroidectomy, along with review of literature.

Keywords Axillary lymph node metastasis · Hürthle cell carcinoma of the thyroid · ^{18}F -FDG PET/CT · Recurrence

Introduction

Differentiated thyroid carcinoma is the most common thyroid carcinoma, associated with an excellent prognosis and indolent course. Larger primary tumor size, extracapsular extension, certain histological variants (namely tall cell, Hürthle cell, and insular variants), older age, and distant metastases have all been identified as risk factors for poorer prognosis, often with a cumulative effect. Distant metastasis is less common with an incidence of 4%, with an overall risk lowest for papillary thyroid carcinoma (2%) and highest for follicular (11%) and Hürthle cell carcinomas (12%) [1]. Metastases to regional lymph nodes are common. However, metastasis to the axillary lymph nodes (ALN) is very unusual. It is generally seen in the context of disseminated disease. The web search of Pubmed in English literature revealed only 25 cases of ALN metastases from thyroid carcinoma so far. Of which, only one case was from Hürthle cell carcinoma [2]. Here, we report a rare case of Hürthle cell carcinoma presenting with a solitary

axillary lymph node metastasis, 17 years after thyroidectomy. The literature available on ALN metastases from thyroid carcinoma is also being discussed.

Case Presentation

Forty-seven-year-old male presented with a left sided neck swelling for 2 months. On USG (ultrasonography) neck, a 3 × 3 cm nodule was noted in left lobe of thyroid. FNAC revealed Bethesda VI, positive for papillary thyroid carcinoma (PTC). Patient underwent near total thyroidectomy. Histopathology revealed a 2.5 × 2.0 cm nodule, positive for Hürthle cell carcinoma with vascular invasion. Serum thyroglobulin (Tg) level was 25 ng/mL (reference range = undetectable–52 ng/mL). Forty-eight hours ^{131}I -whole body scan (WBS) showed a large amount of remnant thyroid activity (uptake 6%). Patient received 1.67 GBq (45 mCi) of ^{131}I therapy. Follow-up ^{131}I -WBS, 6 months later, showed no abnormal focus of tracer uptake indicating that the remnant was ablated. Patient was started on suppressive dose of thyroxine (150 µg). Patient was asymptomatic for a period of 15 years with TSH level varying between 0 and 1.5 µIU/mL (normal range: 0.4–4.5 µIU/mL) and Tg level between 0 and 4 ng/mL (normal range 0–52 ng/mL). He developed a centimeteric subcutaneous nodule in the left side of neck with raised serum Tg level of 10 ng/mL.

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Fig. 1 ^{18}F -FDG PET/CT images. MIP image **a** shows focal increased tracer uptake in the right axilla. Transaxial fused PET/CT **b** and CT **c** images shows increased tracer uptake with a SUVmax value of 2.5, in an enlarged right level I axillary lymph node measuring 1.5×1.0 cm. Also noted were reactive hypermetabolic mediastinal lymph nodes

Excision biopsy of the nodule was positive for poorly differentiated carcinoma thyroid. IHC was positive for TTF and Tg and negative for calcitonin (Ctn). Patient was disease free for another 2 years when he presented again with raised Tg level of 86 ng/mL. USG neck evaluation did not reveal any abnormality. High-resolution computed tomography (HRCT) chest showed no abnormal lung nodules. ^{18}F -FDG PET/CT was hence advised to look for the site of metastases. After 45 min of injection of 370 MBq (10 mCi) of ^{18}F -FDG, scan was acquired. Maximum intensity projection (MIP) image revealed a small focus of increased tracer uptake noted in the right axilla region. On transaxial sections, a 1.5×1 -cm level I right axillary lymph node was noted with increased ^{18}F -FDG uptake having a SUVmax value of 2.5 (Fig. 1). Few reactive mediastinal lymph nodes with increased tracer uptake as noted. No other abnormal metabolically active lesion was noted in the body, and excision biopsy

of the right axillary lymph node was advised. Result was positive for metastatic carcinoma, Figure 2a shows trabeculae of malignant Hürthle cells. Immuno-histochemistry (IHC) was strongly positive for Tg and overall features compatible with primary from thyroid (Fig. 2b). Patient then underwent right axillary lymph node dissection (ALND). Histopathology of right axillary lymph node specimen was negative for tumor (0/16 lymph nodes). Post dissection, serum Tg level dropped to 6 ng/mL. This case is a rare presentation of Hürthle cell carcinoma of the thyroid metastases to solitary axillary lymph node after a long gap of 17 years.

Discussion

On reviewing all the cases already published and the present case, described in Table 1, we found that the mean age of these patients was 52 years with range from 19 to 76 years. Thyroid

Fig. 2 **a** Photomicrograph from right axillary lymph node shows trabeculae of malignant Hürthle cells H&E $\times 200$. **b** The tumor cells show strong cytoplasmic positivity for thyroglobulin

Table 1 Details of the cases reported with thyroid cancer with metastases to axillary lymph nodes

Year	Author	Age/ sex	Histology	Differentiation	Time to ALN appearance	ALN detection	Tumor markers	Outcome
2017	Present study	47/M	FTC	Hürthle cell	Rec 17 years	¹⁸ F-FDG PET/CT	Tg:86 ng/dL	ALND
2015	Kamaleshwaran et al. [3]	38/F	PTC	NA	concurrent	¹³¹ I WBS	NA	ALND
2015	Hafez et al. [4]	61/M	PTC	NA	Rec 18 mo	CT	NA	ALND
2014	Singhal N et al. [5]	19/F	PTC	Well differentiated	concurrent	¹⁸ F-FDG PET/CT	NA	Disease free: 2 mo
2014	Singhal N et al. [5]	58/F	PTC	Tall cell	Rec 11 years	CT	Tg: 0.02 ng/dL	ALND
2014	Cummings et al. [6]	56/F	PTC	Well differentiated	Rec 8 years	Breast MRI	Tg: 1859 ng/dL	ALND
2014	Cummings et al. [6]	59/M	MTC	NA	Rec 3 mo	¹⁸ F-FDG PET/CT	Ctn: 2113 pg/mL	LSCLN recurrence post 1 mo of ALND
2014	Eun Jung Koo et al. [7]	68/M	PTC	Follicular	Rec 17 mo	CT and ¹⁸ F-FDG PET/CT	Tg: >1000 ng/dL	ALND
2012	Machado et al. [8]	76/M	PTC	Well differentiated	Rec 7 years	CT	Tg: 8814 ng/dL	ALND
2012	Chiofalo et al. [2]	65/M	FTC	Hürthle cell, signet cell	concurrent	CT	Tg: 128,150 ng/d- L	ALND
2012	Elboga U et al. [9]	64/M	PTC	Classical	Rec 14 years	¹⁸ F-FDG PET/CT	Tg:292 ng/dL	ALND
2011	Damle et al. [10]	37/M	PTC	Follicular	Rec 3 years	¹³¹ I WBS	Tg: 75 ng/dL	NA
2011	Krishnamurthy et al. [11]	64/F	PTC	Tall cell	Rec 6 years	Physical examination	Tg: 176 ng/dL	Disease free: 6 mo
2009	Kepenecki et al. [12]	63/F	PTC	Well differentiated	Concurrent	US mammography	Tg: 123 ng/dL	NA
2009	Angeles-Angeles et al. [13]	58/F	PTC	Insular	Rec 17 years	Physical examination	NA	Metastases to breast 3 mo later then unknown
2007	Nakayama et al. [14]	21/M	PTC	Well differentiated	Concurrent	CT	Tg: 800 ng/dL	ALND
2006	Ers et al. [15]	62/F	PTC	NA	Rec 5 years	¹⁸ F-FDG PET/CT	Tg: 274 ng/dL	Disease free: 10 years
2004	Koike et al. [16]	46/F	PTC	Well differentiated	Rec 5 years	US mammography	NA	Death 8 mo post ALND
2004	Shehadeh et al. [17]	38/F	SMECE	NA	Concurrent	CT chest	NA	Palliative treatment
2003	Lal et al. [18]	24/M	PTC	Poorly differentiated	Rec 41 years	NA	NA	Death 1 mo post ALN metastases
2003	Lal et al. [18]	59/M	MTC	Poorly differentiated	Concurrent	CT	Ctn: 2343 pg/mL	ALND
2003	Lal et al. [18]	45/M	PTC	Poorly differentiated	Concurrent	NA	NA	Death 10 mo post ALN metastases
2002	Mianagawa et al. [19]	52/M	MEC	NA	Concurrent	CT chest, MRI	CEA:239.7 µg/L	Death 2 mo post ALN metastases
1998	Chen et al. [20]	66/F	PTC	Well differentiated	Concurrent	NA	NA	NA
1996	Ueda et al. [21]	45/F	PTC	NA	Rec 7 years	^{99m} Tc scan	NA	NA
1993	Mizukami et al. [22]	58/M	MEC	Poorly differentiated	Rec 7 mo	NA	Within normal limit	Disease free: 10 mo

ALN axillary lymph node, CEA carcinoembryonic antigen, FTC follicular thyroid carcinoma, L left, MEC mucoepidermoid carcinoma, SCLN supraclavicular lymph node, SMECE sclerosing mucoepidermoid carcinoma with eosinophilia, WBS whole body scan, Rec recurrent, Mo months

cancer metastasis to ALN was seen slightly higher among males than in females with M/F ratio (1.16:1). Of the reported cases, most common histological subtype seen was PTC ($n = 19$), followed by MTC ($n = 2$), rarer histopathological variants such as sclerosing mucoepidermoid carcinoma with

eosinophilia ($n = 1$), primary mucoepidermoid carcinoma ($n = 2$). Only one case of Hürthle cell variant of FTC with metastases to ALN is reported [2]. As seen from Table 1, ALN metastases can occur either concurrently or present as recurrence lesion after certain years. When analyzed, the

average duration for recurrence was about 10 years, with a wide range of 3 months to 41 years. Average duration of 10 years is a long period. This reinforces the fact that long-term follow-up of thyroid cases is strongly recommended. Regarding the tumor markers, wide variation in ranges were noted (serum Tg levels varied from 0.02 to 128,150 ng/mL). Raised serum calcitonin and CEA levels were noted in cases of MTC with metastases to axillary lymph nodes. Various modalities were used for detection of ALN metastases such as ^{131}I -WBS, ^{18}F -FDG PET/CT, CT, MRI, USG, or mammography or even by physical examination. ^{18}F -FDG PET/CT was helpful in detection of ALN metastases in six cases, reported in literature. Out of the 22 patients whose outcome was known, 22 patients underwent ALND and 4 patients died.

Few hypotheses have been proposed to explain the unusual spread. Ers et al. suggested hematogenous dissemination or retrograde dissemination through regional lymphatic channels [15]. Kepenekci et al. hypothesized obstruction of lymphatic vessels resulting in retrograde dissemination through the regional lymphatic channels as the basis for axillary metastasis in thyroid cancer [12]. Rouviere et al. hypothesized that a communication may be present between the cervical and axillary lymphatics [23]. Rare possibility of malignant degeneration of ectopic thyroid tissue in the axilla has also been reported [24].

In our patient, the malignancy and subsequent recurrence in a subcutaneous nodule in the left side of neck could have caused the axillary lymph node metastasis. Axillary lymph node metastasis is known to be associated with systemic disease and a poor prognosis. Aggressive management of such cases is required such as metastatic axillary lymphadenectomy and/or ^{131}I therapy in cases which are radioiodine avid and have concomitant distant metastasis [10]. This case highlights the importance for long-term follow-up of patients with Hürthle cell carcinoma of thyroid.

Compliance with Ethical Standards

Conflict of Interest The authors Meghana Prabhu, Deepali Jain, Siddhartha Datta Gupta, Chandra Sekhar Bal, Rakesh Kumar declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Human and Animal Rights This chapter does not contain any studies with animals performed by any of the authors.

Informed Consent The institutional review board of our institute approved this retrospective study, and the requirement to obtain informed consent was waived.

Informed consent was obtained from the patient for FDG PET/CT in the study.

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