Clinics in Surgery

Case Report
Published: 11 Apr, 2022

An Extraordinary Case of Recurring LN-Metastatic Papillary Thyroid Cancer

Beatrix Neururer[1#], Lorenza Scarpa[1*#], Gianpaolo Di Santo[1], Henrik Einspieler[1], Rupert Prommegger[2] and Irene J Virgolini[1]*

[1]Department of Nuclear Medicine, Medical University Innsbruck, Austria

[2]Department of Visceral and General Surgery, Sanatorium Kettenbrücke Innsbruck, Austria

[#]These authors contributed equally to this work

Abstract

Papillary Thyroid Cancer (PTC) is a differentiated thyroid cancer and also the most common subtype. The incidence, according to expanding use of imaging techniques, biopsy procedures (mostly fine-needle aspiration) and medical surveillance, along with improved access to healthcare, in the last decades are increased; nevertheless the prognosis is very good, with a life expectancy of 85% after 20 years from thyroidectomy. Almost 15% are more aggressive and can metastasize. Up to 50% PTC spread to cervical lymph nodes but distant metastases (primarily lungs or bone) are very rare. Following surgery, including lymphadenectomy, in case of multifocal localized microcarcinoma (stage pT1a (m)) or up to extensive stage (≥ pT1b) after a positive radioactive iodine uptake scans, therapy with ^{131}I-Nal Radioiodine (RAI) is the most common and effective therapy option. However, PTC may lose the ability to absorb radioiodine and alternative treatment options (such as (re-) surgery, Tyrosinkinase Inhibitors (TKI)) are suitable according to a multidisciplinary decision.

Keywords: Papillary thyroid cancer; Lymph node; Radioiodine resistance; Tyrosinkinase-inhibitor

OPEN ACCESS

Correspondence:
Beatrix Neururer, Department of Nuclear Medicine, Medical University Innsbruck, Austria, Tel: 0043-512-504-80988; Fax: 6722683; E-mail: beatrix.neururer@tirol-kliniken.at

Lorenza Scarpa, Department of Nuclear Medicine, Medical University Innsbruck, Austria, Tel: 0043-512-504-83198; Fax: 6722683; E-mail: lorenza.scarpa@tirol-kliniken.at

Received Date: *10 Feb 2022*
Accepted Date: *05 Apr 2022*
Published Date: *11 Apr 2022*

Citation:
Neururer B, Scarpa L, Di Santo G, Einspieler H, Prommegger R, Virgolini IJ. An Extraordinary Case of Recurring LN-Metastatic Papillary Thyroid Cancer. Clin Surg. 2022; 7: 3476.

Introduction

Differentiated thyroid cancer is the most common and increasing endocrine malignancy and PTC is the most common histologic type with more than 80% of all cases [1,2]. For patients diagnosed with PTC there is usually a very good long term and disease-specific survival [1,3]. The most used staging stratification system worldwide is the TNM staging system, which is based on tumor type, tumor extent, and evidence of Lymph Node (LN) and/or visceral metastases [1,4]. Although PTC is regarded as an indolent tumor, 30% to 80% of cancer cells will metastasize to locoregionally LNs and this becomes then a negative predictive value of prognosis [5]. LN metastasis is an important indicator of local recurrence and distant metastasis [6]. Here, we report a case of PTC with recurrent LN metastasis in a 63-year-old man.

Case Presentation

Seven years ago, a 62-year-old male patient was referred to the thyroid outpatient ambulance due to an incidentally mass in his neck/swollen LN right cervical. A neck ultrasound, thyroid planar scintigraphy and a magnetic resonance imaging diagnosed a suspicious thyroid node and pathologic LN right cervical (Figures 1A-1E). Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) Positron Emission Tomography/Computed Tomography (PET/CT) confirmed glucose hypermetabolic LNs right cervical and mediastinal (Figure 2A). After total thyroidectomy and neck dissection the diagnosis of multifocal PTC with LN metastases (Stage: pT3m (1.3 cm), pN1a (6/19), L0 V0 PN0; BRAF positive, loss of p27, cyclin D1 positive) was confirmed. Over the last years the patient received 5 high dosage RAI (accumulated activity 27 GBq) (Figure 3) and twice LN resections due to LN recurrence (Figures 2B-2D). The patient was repeatedly restaged (Figure 2E, 2F), a rising of tumor marker Thyroglobulin (TG) (Figure 4) and also further ^{18}F-FDG-positive, but radioiodine negative LN metastases were reported (Figure 2G). In view of an asymptomatic patient and any kind of progression at the last control a "watch and wait strategy" was temporarily decided.

Discussion

Generally, PTC has an excellent prognosis with a 10-year survival over 90% after initial surgery

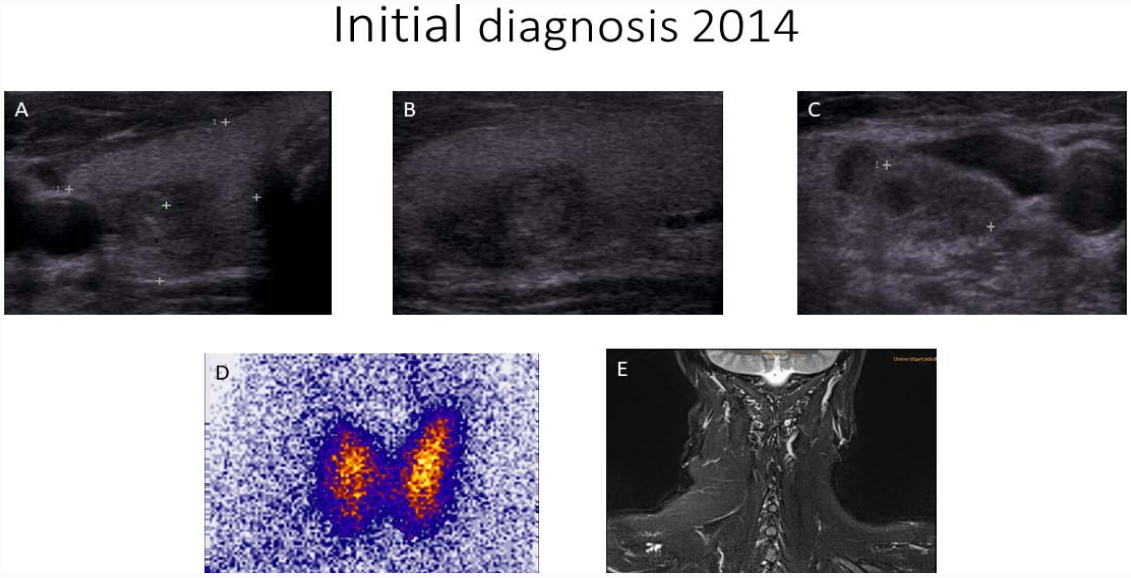


Figure 1: Initial diagnosis 2014: (A, B) ultrasound of thyroid node. (C) Ultrasound of cervical lymph node. (D) Thyroid scintigraphy. (E) Magnetic resonance of neck.

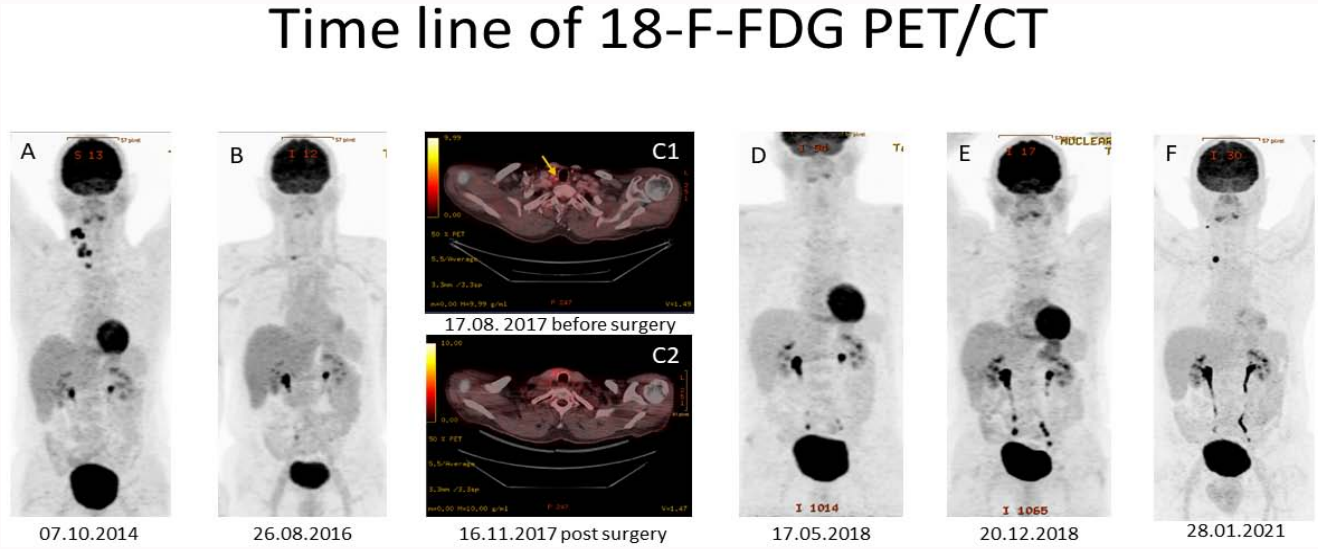
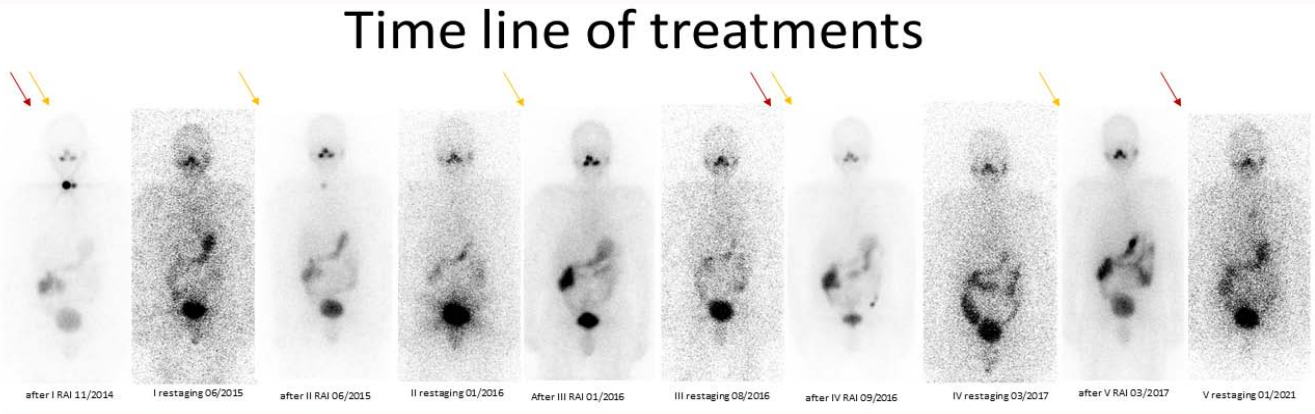


Figure 2: (A) multiple LN-metastases cervical & mediastinal. (B) LN- metastases paratracheal. LN- metastasis paratracheal before (C1) and after (C2) LN-resection. (D, E) normal PET finding. (F) LN- metastases cervical & mediastinal.

[7]. Adverse prognostic factors, such as male gender, age over 55 years, tumor size, LN metastasis are correlating with an increased recurrence rate and mortality [8]. The BRAF mutation, presented in the histology of our patient, like in approximately 45% of all papillary thyroid carcinoma, and the upregulation of biomarker cyclin D1 and the loss of p27 are associated with more aggressive tumor behavior, increasing progression and recurrence [9,10]. Surgery is usually the first-line therapy, where the extension dependents on size of primary tumor and presence of LN metastasis. An oral administered RAI is usually recommended subsequent to surgery. Our patient underwent a total thyroidectomy with concomitant lateral neck dissection, two re-resections of further cervical LN metastasis and received five times RAI with a total activity of 27 GBq. The presence of LN metastasis, especially in the lateral compartment is a significant risk factor for locoregional recurrence, distant metastasis and shorter survival [11]. Two years later our patient presents an increase of thyroglobulin and again suspects LN sites, however, with a negative radioactive iodine accumulation on ^{131}I-whole-body scan and significant uptake on ^{18}F-FDG-PET/CT. The prognosis of PTC becomes significantly less favorable when the tumor no longer absorbs radioiodine as further therapy with radioiodine is no longer possible [12]. According to the review of Mohamed Aashiq et al. [13] there are different approaches in the management of radioiodine-refractory thyroid cancer. If locoregionally relapsed, surgery is still the most commonly performed therapy, but in our case after comprehensive neck dissection and two re-resections this option has nearly been exhausted, due to postoperative complications related to scar tissue but is still discussed, because of the good performance status of our patient. Active surveillance and watchful waiting while TSH suppression, in case of asymptomatic disease, low tumor burden or tumor size (<1 cm) and minimally progression can be employed [13]. The presence of small (<8 mm) and asymptomatic metastatic LN after radioiodine therapy



Treatment	Surgery	I RAI	II RAI	III RAI	Surgery	IV RAI	V RAI	Surgery
Date	14.10.2014	18.11.2014	08.06.2015	13.01.2016	01.09.2016	07.09.2016	20.03.2017	07.09.2017
Dosis (MBq)		6281	5905	5300		5456	4087	
	total thyroidectomy + LN-dissection				18-F-FDG positive LN-resection			18-F-FDG positive LN-resection

Figure 3: Time line of treatments. Red arrow: Surgery, Yellow arrow: RIT.

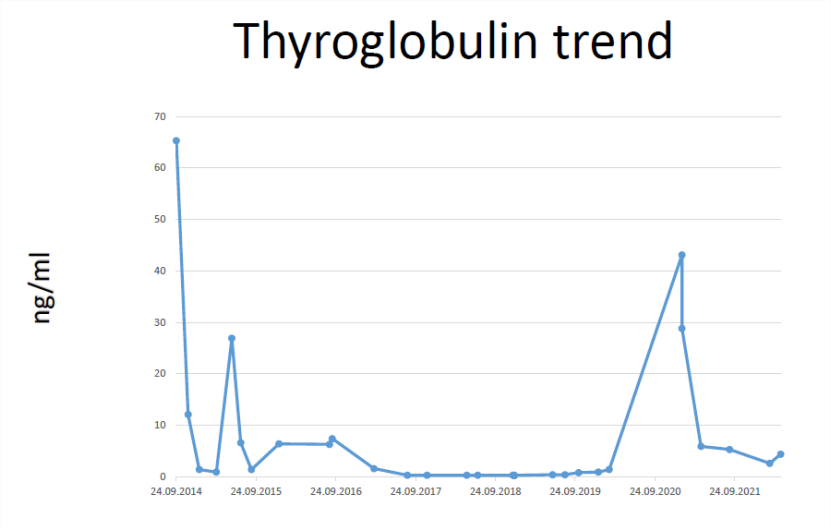


Figure 4: Trend of tumor marker thyroglobulin.

with previous neck dissection and/or small (<1 cm) pulmonary nodules can be followed up for years with sonography and axial imaging. Other imaging modalities, such as ^{18}F-FDG PET/CT, and thyroglobulin levels in TSH-suppressed patients can also be used to assess disease progression [13]. Another therapy option is the target therapy using TKI's. Its efficiency is based on the involvement of thyrosine kinase MAPK signaling pathway, whose degree correlated with cellular dedifferentiation in thyroid cancers, which causes tumor progression correlated with more aggressive growth, metastasis, loss of iodide uptake, or unresponsiveness to RAI [13]. Additional novels therapies, such as multikinase inhibitors for radioiodine resistant thyroid cancer, are part of different clinical trials and could be a future perspective. Novel therapies with highly selective TKI for VEGFR2 with excellent antitumor effects in various types of solid tumors in combination with an autophagy inhibitor may be a useful therapeutic strategy for refractory radioiodine resistant PTC [14]. Optional drug therapy with TKI`s in case of radioiodine-refractory with a well-adjusted balance between efficacy and adverse effects is desirable [15].

Conclusion

RAI contributes to the good prognosis of differentiated thyroid carcinoma also in metastatic in addition to the usually slow tumor growth and the good surgery results. The interdisciplinary therapy of differentiated thyroid carcinoma is based on individual risk and according to the current guidelines.

References

1. Filetti S, Durante C, Hartl D, Leboulleux S, Locati LD, Newbold K, et al. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2019;30(12):1856-83.

2. Abdullah MI, Junit SM, Ng KL, Jayapalan JJ, Karikalan B, Hashim OH. Papillary thyroid cancer: Genetic alterations and molecular biomarker

investigations. Int J Med Sci. 2019;16(3):450-60.

3. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26:1-133.
4. Tuttle RM, Haugen B, Perrier ND. Updated American joint committee on cancer/tumor-node-metastasis staging system for differentiated and anaplastic thyroid cancer (eighth edition): What changed and why? Thyroid. 2017;27:751-6.
5. Feng JW, Qin AC, Ye J, Pan H, Jiang Y, Qu Z. Predictive factors for lateral lymph node metastasis and skip metastasis in papillary thyroid carcinoma. Endocr Pathol. 2020;31(1):67-76.
6. Zhao QZ, Ming J, Liu C, Shi L, Xu X, Nie X, et al. Multifocality and total tumor diameter predict central neck lymph node metastases in papillary thyroid microcarcinoma. Ann Surg Oncol. 2013;20:746-52.
7. Malterling RR, Andersson RE, Falkmer S, Falkmer U, Niléhn E, Järhult J. Differentiated thyroid cancer in a Swedish country--long-term results and quality of life. Acta Oncol. 2010;49(4):454-9.
8. Yasuhiro Ito, Kudo T, Kobayashi K, Miya A, Ichihara K, Miyauchi A. Prognostic factors for recurrence of papillary thyroid carcinoma in the lymph nodes, lung, and bone: Analysis of 5,768 patients with average 10-year follow-up. World J Surg. 2012;36(6):1274-8.
9. Howell GM, Carty SE, Armstrong MJ, Lebeau SO, Hodak SP, Coyne C, et al. Both BRAF V600E mutation and older age (>65 years) are associated with recurrent papillary thyroid cancer. Ann Surg Oncol. 2011;18(13):3566-71.
10. Cheng S, Serra S, Mercado M, Ezzat S, Asa SL. A high-throughput proteomic approach provides distinct signatures for thyroid cancer behavior. Clin Cancer Res. 2011;17(8):2385-94.
11. Hyun SM, Song HY, Kim SY, Nam SY, Roh JL, Han MW, et al. Impact of combined prophylactic unilateral central neck dissection and hemithyroidectomy in patients with papillary thyroid microcarcinoma. Ann Surg Oncol. 2012;19(2):591-6.
12. Schlumberger M, Brose M, Elisei R. Definition and management of radioactive iodine-refractory differentiated thyroid cancer. Lancet Diabetes Endocrinol. 2014;2:356-8.
13. Aashiq M, Silverman DA, Na'ara S, Takahashi H, Amit M. Radioiodine-refractory thyroid cancer: Molecular basis of redifferentiation therapies, management, and novel therapies. Cancers. 2019;11:1382.
14. Meng X, Wang H, Zhao J, Hu L, Zhi J, Wei S, et al. Apatinib inhibits cell proliferation and induces autophagy in human papillary thyroid carcinoma via the PI3K/Akt/mTOR signaling pathway. Front Oncol. 2020;10:217.
15. Laursen R, Wehland M, Kopp S, Pietsch J, Infanger M, Grosse J, et al. Effects and role of multikinase inhibitors in thyroid cancer. Curr Pharm Des. 2016;22(39):5915-26.