Incidental Detection of Occult Thyroid Carcinoma with $^{11}$C-Choline PET/CT for High Risk Prostate Cancer

Adama Ouattara a*, Tiago Ribeiro de Oliveira a*, Serge Holz a
Hannes Van den Bossche a, David Strybol b, Christophe Assenmacher c
Wouter Everaerts a, Gert De Meerleer d, Steven Joniau a

Department of a Urology, b Pathology and d Radiation Oncology, University Hospitals Leuven; c Medicine Teaching Programmes, Katholieke Universiteit Leuven, Leuven, Belgium.

*These authors contributed equally to the manuscript.

Key Words
Positron-emission tomography • Prostate cancer • Thyroid

Abstract
We report a case of a 65-year-old male patient with high-risk prostate cancer, re-staged with $^{11}$C-choline positron emission tomography/computed tomography (PET/CT) for prostate specific antigen recurrences 3 years after radical prostatectomy and adjuvant radiation therapy. In addition to 2 suspicious presacral lymph nodes which were resected and proven to be metastatic, PET/CT revealed a very high uptake in a calcified thyroid nodule. Evaluation with fine needle aspiration was suspicious for thyroid carcinoma and the patient underwent total thyroidectomy, confirming a non-metastatic encapsulated follicular variant of papillary thyroid carcinoma. To our knowledge, this is the first report of a thyroid cancer diagnosed with $^{11}$C-choline PET/CT for prostate cancer staging.

Case Report
A 65-years-old male patient, without relevant past medical history, was diagnosed with a clinically low-risk prostate cancer [Gleason 6 (3 + 3), cT2a with prostate specific antigen (PSA) of 4 ng/ml] at the end of 2009. After discussion of the possible treatment options, the patient opted for active surveillance. A sudden rise of PSA to 8 ng/ml at 6 months follow-up led to a repeat ultrasound-guided transrectal prostate biopsy and multiparametric prostate magnetic resonance imaging (MRI), revealing high-risk locally advanced prostate cancer [cT3b, Gleason 8 (4 + 4) adenocarcinoma]. Staging with computed tomography (CT) did not reveal regional lymph node involvement or distant metastasis, and the patient underwent a non-nerve sparing open radical prostatectomy with superextended pelvic lymphadenectomy. Pathological examination of the prostatectomy specimen identified a pT3b N0 (0/17 nodes positive) M0 R0 Gleason 9 (4 + 5) prostate cancer with perineural and lymphovascular invasion. PSA was undetectable at 3 months follow-up. Adjuvant external beam radiation therapy (66 Gy) to the prostatic fossa was delivered 6 months after surgery.

Due to PSA progression 3 years after surgery and adjuvant radiation therapy, the patient underwent re-staging with $^{11}$C-choline positron emission tomography/computed tomography (PET/CT) (1207.0MBq $^{11}$C-choline IV and Ultravist® 370:120ml contrast IV, abdominal and thorax PET-scan and CT-scan after 5 minutes), revealing two highly suspicious slightly hypermetabolic presacral (mesorectal) lymph nodes and a very high uptake on a calcified nodule on the left lobe of the thyroid (fig. 1).
The patient underwent a salvage lymphadenectomy, targeted to the presacral nodes, with pathology showing 2 positive nodes with tumor diameters of 9 and 4 mm. Despite that, the PSA value did not decline (preoperative value of 0.6 vs. 0.77 ng/ml 2 months post-salvage surgery). A repeat $^{11}$C-choline PET/CT 8 months post-salvage surgery with a PSA of 1.74 ng/ml showed a new lesion behind the psoas muscle in the right presacral area. The patient underwent external beam radiotherapy to the pelvis (54 Gy), with a selective boost to the suspect node (60 Gy) and concomitant/adjuvant androgen deprivation therapy for 2 years. His last PSA was 0.03 ng/ml.

Investigation of the hypermetabolic thyroid focus with fine needle aspiration was suspicious for thyroid carcinoma. The patient underwent a radical thyroidectomy, with the specimen revealing a non-metastatic encapsulated follicular variant of papillary thyroid carcinoma (fig. 2), with 15 mm of maximum diameter and 3 negative lymph nodes (T2N0M0).

**Discussion**

Over the past few years, the use of PET/CT for the detection and evaluation of oncologic disease has become more frequent [1]. This novel imaging technique combines the anatomic resolution of CT scanning with the spatial distribution of metabolic activity of PET scanning, allowing the identification of slight changes in the normal metabolic pattern of organs [1, 2]. Choline, a quaternary ammonium present on the phospholipids of the cellular membrane, is an optimal indicator of cell multiplication and choline marked with either $^{11}$C (carbon 11) or $^{18}$F (fluorine 18) is therefore widely used as a radiolabel for PET/CT scanning [2].

**Fig. 1.** Results of the $^{11}$C-choline PET/CT at the time of re-staging, showing highly suspicious presacral lymph nodes (black arrows) and a very high uptake on a calcified nodule on the left lobe of the thyroid (white arrows): A. Whole-body coronal section; B. Pelvic axial section; C. Thyroid axial section.
PET/CT is nowadays accepted as part of several investigation algorithms in oncology, including prostate cancer where it occupies an important role in the detection of oligo-metastatic lymph nodes or bone metastases before they become apparent on conventional imaging [3–5]. Our patient underwent staging with $^{11}$C-choline PET/CT for a sustained rise of PSA after radical prostatectomy and adjuvant external beam radiation therapy to the prostatic fossa for a locally advanced high-risk prostate cancer.

The incidence of thyroid cancer has been increasing over the past years, mainly due to an increase in the detection of small subclinical lesions [6]. The incidental detection of an occult thyroid carcinoma in patients without previous evidence of thyroid disease and under evaluation due to other malignancies is not uncommon [6]. Although PET/CT is not classically used for the detection of thyroid cancer, the value of fluorodeoxyglucose (FDG) PET in the management of thyroid cancer has progressively been recognized, namely for follow-up after treatment [7]. Despite that, there is currently few evidence on the tropism of thyroid cells for choline. Wu et al. reported a small series of patients with thyroid carcinoma, previously evaluated with whole-body $^{18}$F FDG PET, which underwent regional imaging with $^{11}$C-choline PET/CT. The authors concluded that $^{11}$C-choline PET/CT may be a useful complement to $^{18}$F FDG PET in the detection of thyroid cancer and its metastasis [8].

The consolidation of $^{11}$C and $^{18}$F choline PET/CT as useful tools to stage prostate cancer in the presence of biochemical recurrence has raised the level of experience on this functional imaging modality and has led to a higher rate of detection of incidental malignant lesions in several organs, with the potential to modify treatment options and disease prognosis [9]. Treglia et al. [10] have reported the detection of thyroid incidental lesion on an $^{18}$F-choline PET/CT at the time of re-staging a prostate cancer patient, later to be defined as a benign thyroid neoplasm. We describe the first case of an incidental detection of a thyroid cancer with an $^{11}$C-choline PET/CT used to re-stage a high-risk locally advanced prostate cancer. In our patient, the early detection of the thyroid cancer allowed a timely curative procedure, with clear benefit for the patient.

In conclusion, this case reinforces the potential use of choline PET/CT in the management of several malignancies other than prostate cancer. Moreover, although more evidence must be obtained on the sensitivity and specificity of choline PET/CT in the diagnosis of particular cancers, it is our believe that, with the growing use of this promising imaging modality, urologists and oncologists must be aware of its potential to identify incidental malignant lesions, in order to provide a higher level of care for their patients.

Fig. 2. Histology of radical thyroidectomy specimen: follicular variant of papillary thyroid carcinoma.
References

1. Saif MW, Tzannou I, Makrilia N, Syrigos K: Role and cost effectiveness of PET/CT in management of patients with cancer. Yale J Biol Med 2010;83:53–65.
2. Cuccurullo V, Di Stasio GD, Evangelista L, Castoria G, Mansi L: Biochemical and pathophysiological premises to positron emission tomography with choline radiotracers. J Cell Physiol 2017;232:270–275.
3. Morigi JJ, Fanti S, Murphy D, Hofman MS: Rapidly changing landscape of PET/CT imaging in prostate cancer. Curr Opin Urol 2016;26:493–500.
4. Umbehr MH, Müntener M, Hany T, Sulser T, Bachmann LM: The role of $^{11}$C-choline and $^{18}$F-fluorocholine positron emission tomography (PET) and PET/CT in prostate cancer: a systematic review and meta-analysis. Eur Urol 2013;64:106–117.
5. Mottet N, Bellmunt J, Briers E: Guidelines on prostate cancer. European Association of Urology 2016.
6. Davies L, Welch HG: Increasing incidence of thyroid cancer in the United States, 1973–2002. JAMA 2006;295:2164–2167.
7. Ciarallo A, Marcus C, Taghipour M, Subramaniam RM: Value of fluorodeoxyglucose PET/computed tomography patient management and outcomes in thyroid cancer. PET Clin 2015;10:265–278.
8. Wu HB, Wang QS, Wang MF, Li HS: Utility of C-choline imaging as a supplement to F-18 FDG PET imaging for detection of thyroid carcinoma. Clin Nucl Med 2011;36:91–95.
9. Welle CL, Cullen EL, Peller PI, Lowe VI, Murphy RC, Johnson GB, Binkovitz LA: $^{11}$C-choline PET/CT in recurrent prostate cancer and nonprostatic neoplastic processes. Radiographics 2016;36:279–292.
10. Treglia G, Giovannini E, Mirk P, Di Franco D, Oragano L, Bertagna F: A thyroid incidentaloma detected by $^{18}$F-choline PET/CT. Clin Nucl Med 2014;39:e267–269.