### Abstract

Thyroglobulin-elevated negative iodine scan (TENIS) syndrome represents a significant diagnostic and therapeutic challenge. Highly sensitive imaging modalities are required to help in the localization of disease, treatment planning, and prognostication. When compared to other imaging modalities, F-18 fluorodeoxyglucose positron-emission tomography–computed tomography has superior sensitivity and specificity in localizing the disease in this subset of patients. Tumor thrombus of thyroid cancer extending into the great vein is a very rare occurrence and management criteria have not been well established yet. We present a case of TENIS syndrome with tumor thrombus in the superior vena cava.

**Keywords:** Fluorodeoxyglucose positron-emission tomography–computed tomography, superior vena cava tumor thrombus, thyroglobulin-elevated negative iodine scan

## Introduction

Differentiated thyroid cancer (DTC) is the most frequent thyroid cancer, representing 1% of all malignant tumors. In general, it has an excellent prognosis; however, recurrence is seen in 20% of patients.<sup>[1]</sup> After risk stratification and initial surgery followed by high-dose 1311 ablation, follow-up monitoring consists of neck ultrasonography (USG), evaluation of serum thyroglobulin (Tg) levels and anti-Tg antibodies, and 131- iodine whole-body scans (WBSs). Undetectable levels of serum Tg levels suggest a successful treatment. A stimulated Tg level of >10 ng/ml has been considered biochemically incomplete response and recommended as a cutoff point. Often in these patients, a scan following the empirical administration of a therapeutic dose of 131-I may demonstrate iodine avid disease,[2] which has been explained by the higher sensitivity of post-therapy WBS. However, post-therapy scan may still continue to be negative suggesting Tg-elevated negative iodine scan (TENIS) syndrome. Alternative imaging is then indicated for the localization of disease in this subset of patients.<sup>[3]</sup> When compared to other alternative imaging modalities, F-18 fluorodeoxyglucose (FDG)

positron-emission tomography/computed tomography (PET/CT) has a sensitivity of 85%–94% and specificity of 90%–95%<sup>[4]</sup> The American Thyroid Association 2015 guidelines for DTCs recommend further imaging with FDG-PET/CT in patients who are Tg positive (10 ng/mL) and have negative radioiodine scan.<sup>[5]</sup> Here, we present a rare case of TENIS with superior vena cava (SVC) tumor thrombus to substantiate the role of F18-FDG whole-body PET-CT in localization and treatment planning in such situations.

### **Case Report**

A 55-year-old female presented with swelling in the neck for 2 years gradually increasing in size. She underwent USG of the neck which showed a nodule in the left lobe suspicious of malignancy. FNAC was suggestive of Bethesda Classification VI lesion. She then underwent a total thyroidectomy. Histopathology showed a follicular variant of papillary carcinoma further histopathological thyroid. No details were available. She was lost to follow-up since then. She then presented with local recurrence after 4 years. Computed tomography showed a 6 cm  $\times$  6  $cm \times 3.5$  cm mass lesion in the left lobe of the thyroid with an invasion of the internal jugular vein (IJV). She underwent local excision of tumor along with IJV.

How to cite this article: Gadepalli T, Abubacker ZA, Bikkina P, Pasupula MV. A rare case of TENIS presenting with SVC thrombus - Highlighting the role of PET-CT scan. Indian J Nucl Med 2021;36:312-5.

# Tejonath Gadepalli, Zakir Ali Abubacker, Pratyusha Bikkina, Madhu Vijay Pasupula

Department of Nuclear Medicine, Basavatarakam Indo-American Cancer Hospital and Research Institute, Hyderabad, Telangana, India

Address for correspondence: Dr. Tejonath Gadepalli, Department of Nuclear Medicine, Basavatarakam Indo-American Cancer Hospital and Research Institute, Road No. 10, Banjara Hills, Hyderabad - 500 034, Telangana, India. E-mail: tejonathg@gmail.com

Received: 02-02-2021

Accepted: 11-03-2021 Published: 23-09-2021



This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

Histopathology showed tumor deposit of follicular variant of papillary carcinoma thyroid. Subsequently, she received 150 mCi of radioactive iodine. Post-therapy scan showed intense localization of radioiodine in the thyroid bed with no evidence of locoregional or distant spread [Figure 1]. On subsequent follow-up after 6 months, the patient was asymptomatic with elevated serum Tg (2827 ng/ml) and a negative WBS [Figure 2]. She was advised for an F18-FDG whole-body PET-CT scan which showed a metabolically active filling defect in the SVC and left innominate vein [Figure 3] and no other metabolically active disease elsewhere in the body. Being inoperable, the patient

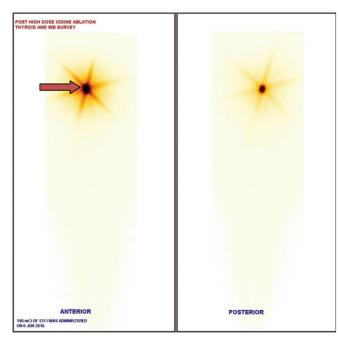


Figure 1: Whole body I-131 scan post 150 mCi of radioiodine administration

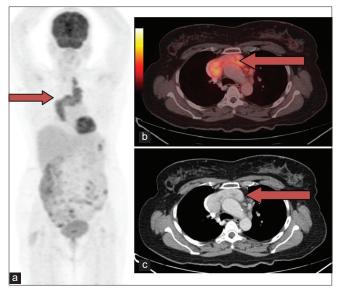


Figure 3: Whole body F18-FDG PET-CT images showing increased metabolic activity in the tumor thrombus of SVC: a) MIP image b) Fused image c) CT image

received External Beam Radiotherapy (EBRT) 60 Gy in 30 fractions for this lesion. A follow-up whole-body FDG PET-CT scan showed partial response as per the PERCIST criteria [Figure 4]. Serum Tg levels also reduced mildly to 2506 ng/ml. Since then, she was on a regular follow-up. PET CT scan after 9 months showed stable disease with serum Tg of 2297 ng/ml [Figure 5]. However, on subsequent follow-up after 12 months, the serum Tg was significantly elevated to 4867 ng/ml. She was then referred again for an FDG whole-body PET-CT scan which showed new areas of tumor thrombus in the upper one-third of the left IJV extending intracranially with a widening of jugular foramen [Figure 6]; however, the SVC thrombus remained stable. The patient continues to be asymptomatic. However, in view of rising Tg levels, she was recently started on tyrosine kinase inhibitors.

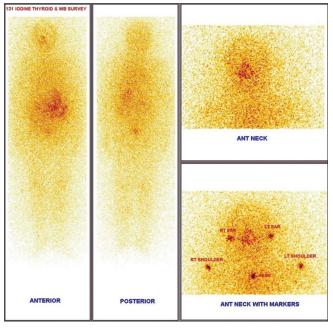


Figure 2: First follow up 3 mCi I131 scan showing no iodine avid disease (Serum thyroglobulin 2827 ng.ml)

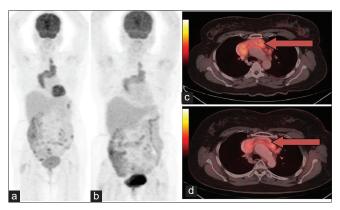


Figure 4: Comparison whole body PET-CT scan before and after external beam radiotherapy (RT): a) MIP image before RT, b) MIP image after RT, c) Fused image before RT and d) Fused image after RT

## Discussion

TENIS syndrome represents a significant diagnostic and therapeutic challenge. A stimulated Tg is a sensitive marker for both residual and recurrent diseases.<sup>[6]</sup> Not uncommonly, during the course of thyroid cancer management, situations arise where there is no clinically evident disease, but serum Tg levels remain detectable or even significantly elevated. WBS is negative in 20% of patients with detectable Tg levels.<sup>[7]</sup> In general, for all practical purposes, a stimulated Tg level of >10 ng/ml has been recommended as a cutoff point to suggest further work-up for disease localization. Alternative imaging modalities are indicated for the localization of disease in this subset of patients. Among these imaging modalities, F-18 FDG PET/CT imaging has the highest sensitivity (85%–94%) and specificity (90%–95%).

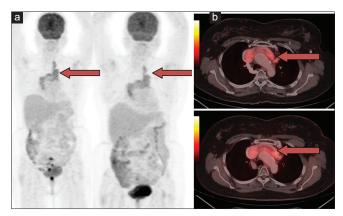


Figure 5: Follow up whole body F-18 FDG PET-CT scan: a) Comparison MIP, b) Fused images comparison

In the present case scenario, F-18 FDG whole-body PET-CT scan showed metabolically active tumor thrombus in the left innominate vein and SVC. Tumor thrombus of thyroid cancer in a major vein is rare with an incidence of 0.2%–3.8%.<sup>[8]</sup> Many of the cases of venous tumor thrombus of thyroid cancer are asymptomatic and accidentally detected on USG or CT scan. However, patients may rarely present with SVC syndrome.<sup>[9]</sup> Only a few reports have shown thyroid cancer patients with tumor thrombus that progresses to the innominate vein, SVC, or intracranial extension beyond IJV.<sup>[10]</sup> Detection of the extent of tumor thrombus is important for treatment planning which may either be radiotherapy or a surgical procedure. Whole-body FDG-PET/CT is an excellent tool for delineation of the tumor extent including vascular tumor invasion.<sup>[11]</sup>

#### Conclusion

TENIS syndrome is a well-established entity posing a significant diagnostic challenge in the management of carcinoma thyroid patients. Whole-body F-18 FDG PET-CT has proved its efficacy for further evaluation of patients with TENIS syndrome as demonstrated in this patient with a rare presentation as tumor thrombus in the superior vena cava.

#### **Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not

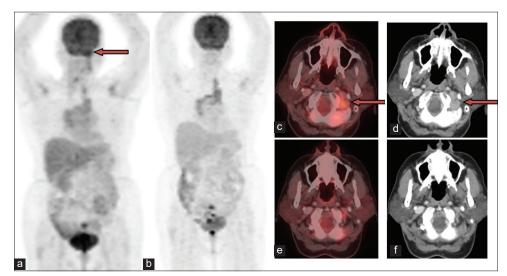


Figure 6: Follow up PET-CT comparison images stable SVC thrombus on MIP images (a,b), Fused (c) and CT (d) images showing new metabolically active tumor thrombus in left upper IJV extending into jugular canal compared to previous scan (e,f) suggesting disease progression.

be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

#### **Financial support and sponsorship**

Nil.

#### **Conflicts of interest**

There are no conflicts of interest.

### References

- Pacini F, Schlumberger M, Dralle H, Elisei R, Smit JW, Wiersinga W, *et al.* European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. Eur J Endocrinol 2006;154:787-803.
- 2. Pineda JD, Lee T, Ain K, Reynolds JC, Robbins J. Iodine-131 therapy for thyroid cancer patients with elevated thyroglobulin and negative diagnostic scan. J Clin Endocrinol Metab 1995;80:1488-92.
- 3. Silberstein EB. The problem of the patient with thyroglobulin elevation but negative iodine scintigraphy: The TENIS syndrome. Semin Nucl Med 2011;41:113-20.
- Reske SN, Kotzerke J. FDG-PET for clinical use. Eur J Nucl Med 2001;28:1707-23.
- 5. 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;26:1-33.

- Mazzaferri EL, Robbins RJ, Spencer CA, Braverman LE, Pacini F, Wartofsky L, *et al.* A consensus report of the role of serum thyroglobulin as a monitoring method for low-risk patients with papillary thyroid carcinoma. J Clin Endocrinol Metab 2003;88:1433-41.
- Dong MJ, Liu ZF, Zhao K, Ruan LX, Wang GL, Yang SY, et al. Value of 18F-FDG-PET/PET-CT in differentiated thyroid carcinoma with radioiodine-negative whole-body scan: A meta-analysis. Nucl Med Commun 2009;30:639-50.
- Kobayashi K, Hirokawa M, Yabuta T, Fukushima M, Kihara M, Higashiyama T, *et al.* Tumor thrombus of thyroid malignancies in veins: Importance of detection by ultrasonography. Thyroid 2011;21:527-31.
- 9. Bordigoni L, Blin D, Magnan PE, Giudicelli R, Fuentes P. Ectatic tumoral thrombosis of the superior vena cava revealing thyroid cancer. Ann Chir 1992;46:194-8.
- Kawano F, Tomita M, Tanaka H, Nagahama H, Tashiro K, Nakao H, *et al.* Thyroid carcinoma with extensive tumor thrombus in the superior vena cava: A case report. Int J Surg Case Rep 2016;29:25-9.
- 11. Strobel K, Steinert HC, Bhure U, Koma AY, Gassmann N, Stöckli SJ. Tumour thrombus in the superior vena cava from anaplastic carcinoma of the thyroid: FDG-PET/CT imaging findings. Eur J Nucl Med Mol Imaging 2007;34:813.