Case Report

Great cervical venous tumoral thrombosis of melanotic medullary carcinoma thyroid: Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography enabled diagnosis and radiotherapy planning

Mohana Vamsy Chigurupati, Vidya Madiraju[1], Namrata Chigurupati[1], Pawan Gulabrao Shinkar[2], Snehalatha Dhagam[3], Vatturi Venkata Satya Prabhakar Rao[4]

Departments of Surgical Oncology, [1]Radiation Oncology, [2]Radio Diagnosis, [3]Pathology and [4]Nuclear Medicine and Positron Emission Tomography/Computed Tomography, Omega Hospitals, Banjara Hills, Hyderabad, Telangana, India

ABSTRACT

The authors report an extremely rare occurrence of a massive tumor thrombus involving right internal and external jugular veins extending into superior vena cava from a still rarer melanotic medullary carcinoma thyroid in the postoperative follow-up. The case was managed by hypofractionated intensity modulated radiotherapy technique with gratifying results.

Keywords: Hypofractionated radiotherapy, intensity modulated radiotherapy, melanotic medullary carcinoma thyroid, tumor thrombus

INTRODUCTION

Tumor thrombus into major neck veins in medullary carcinoma thyroid is as yet an unreported event. Despite an absent gross local tumor in the neck, such metastatic veno invasive phenomenon has occurred in the post operated follow-up period. Outlining the tumor thrombus and its extent by fluorine-18 fluorodeoxyglucose positron emission tomography computed tomography (F18 FDG PET/CT) and the subsequent management by PET-CT planning based intensity modulated radiotherapy (IMRT) with successful eradication of the tumoral metabolic activity and regression of the thrombus highlights this rare clinical phenomenon.

Address for correspondence:
Dr. Prabhakar Rao Vatturi Venkata Satya, Department of Nuclear Medicine and Positron Emission Tomography/Computed Tomography, OMEGA Hospitals, MLA Colony, Road No: 12, Banjara Hills, Hyderabad - 500 034, Telangana, India.
E-mail: vvs_prabhakar@yahoo.co.uk

Access this article online

Quick Response Code:

Website: www.ijnm.in

DOI: 10.4103/0972-3919.172361

CASE REPORT

A 44-year-old male presented with a mass on the right side of the neck known to have been stable for more than 10 years with a history of the increase in size from past 1 month associated with pain. There were no compressive symptoms and no history of flushing, cardiovascular disturbances, or diarrhea. Clinically, he was in euthyroid status. Past medical history was unremarkable. Physical examination revealed a nodule of 5 cm × 4 cm in the right lobe of thyroid gland with enlargement of level III cervical lymph nodes on the left side. Hematological, biochemical, and thyroid hormonal parameters were within normal limits. High-resolution ultrasonography of neck showed a 4.4 cm × 3.5 cm heterogeneous echo textured nodule right lobe thyroid with multiple calcific specks within. Left lobe also showed multiple small nodules with areas of coarse calcifications. Few lymph nodes noted along the

How to cite this article: Chigurupati MV, Madiraju V, Chigurupati N, Shinkar PG, Dhagam S, Prabhakar Rao VV. Great cervical venous tumoral thrombosis of melanotic medullary carcinoma thyroid: Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography enabled diagnosis and radiotherapy planning. Indian J Nucl Med 2016;31:45-8.

left jugular vein largest measuring 1 cm × 0.7 cm, one of them showing calcific specks. Fine needle aspiration cytology (FNAC) performed showed features suggestive of anaplastic carcinoma with brownish-black pigment. A diagnosis of poorly differentiated malignancy with melanin pigment, possible malignant melanoma was made from the intraoperative frozen section of the tumor and hence a total thyroidectomy with removal of enlarged cervical lymph nodes was performed in one sitting. Gross findings showed enlargement of both lobes of thyroid with blackish discoloration of right lobe [Figure 1a]. Microscopic examination of right lobe thyroid lobe revealed nodularity comprised of polygonal to spindle cells, showing organoid pattern with clumped chromatin, moderate to abundant cytoplasm, with areas of necrosis, focal hemorrhage, and abundant extracellular brownish black melanin pigment. The majority of tumor cells showed intracellular melanin deposition [Figure 1b]. Sections from left lobe of thyroid showed features of medullary carcinoma of thyroid with amyloid production, without melanin pigment. Immunohistochemistry showed positivity with HMB45 in right lobe [Figure 1c] calcitonin in left lobe [Figure 1d]. A final diagnosis of melanotic medullary carcinoma of thyroid with amyloid production was made. Excised lymph nodes showed metastatic medullary deposits.

In view of medullary carcinoma with melanin production, further work-up was done with serum calcitonin whole body iodine 131 meta iodo benzyl guanidine (I 131 MIBG) scan to outline any residual or metastatic foci with an intent to treat with high dose of I 131 MIBG. Serum calcitonin was 8 ng/L and I 131 MIBG scan did not reveal any residual or metastatic localization. Thus, due to nontherapeutic options with MIBG and known radio resistance to radiotherapy of melanotic medullary carcinoma thyroid,[1] patient was kept on close follow-up. One year later, patient presented with diffuse boggy swelling in the right side of neck associated with severe pain radiating to the right ear, however, there was no puffiness of face, engorged veins on the neck or chest wall. Clinical examination revealed a firm diffuse fixed mass along the right jugular region. A F-18 FDG PET/CT was performed which revealed an intensely hypermetabolic hypo dense intraluminal filling defect with an standardized uptake value maximum of 16.61 in the internal jugular vein (IJV), external jugular vein (EJV), right subclavian vein confluencing at the right innominate vein with inferior extension into the superior vena cava (SVC) falling just short of the right atrium suggestive of tumoral thrombus. There was no residual thyroid in the thyroid bed, however, a small metabolically active pretracheal lymph node was noted [Figure 2]. There was no residual mass in the thyroid bed or elsewhere in the neck. There was no hematological evidence of any thrombotic or prothrombotic states. Serum calcitonin was elevated to 300 ng/L FNAC from the solitary pretracheal node revealed metastatic deposit of medullary carcinoma. With limited therapeutic options and impending cardiovascular catastrophe due to large tumor thrombus load, an immediate blunderbuss salvage radiotherapy was given, with F18 FDG PET/CT based IMRT. The field included the metabolically active mass in the IJV and SVC extending up to right atrium along with neck, sparing the adjoining trachea and carotid vessels to prevent carotid artery stenosis and blow out. A hypofractionated technique was employed delivering a cumulative dose of 50 Gy in 20 fractions instead of the conventional 28–25 fractions of 1.8–2 Gy/fractions. The patient tolerated the entire course without any hematological or vascular complications and became symptom-free by the end of the radiation treatment. Patient was kept on clinical follow-up and assessment with F18 FDG PET/ /CT done subsequently revealed complete metabolic regression in the intravascular tumor with significant reduction in the tumor thrombus and better contrast passage through the SVC [Figure 3]. Follow-up at 3 months patient continued to be symptom-free with complete disappearance of the boggy neck swelling. Color Doppler of the

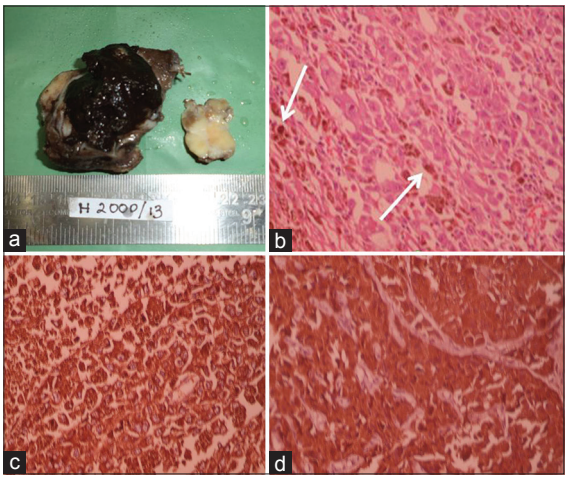

Figure 1: (a) Gross specimen showing nodular enlargement of thyroid with blackish discoloration of the right lobe. (b) Microscopic features showing polygonal to spindle cells, in an organoid pattern with clumped chromatin, abundant cytoplasm, and areas of necrosis, focal hemorrhage, copious extracellular brownish black melanin pigment (arrow). (c) Immunohistochemistry right lobe shows tumor cells with brownish-black pigment showing strong cytoplasmic positivity with HMB45. (d) Immunohistochemistry left lobe shows tumor cells with brownish-black pigment showing strong cytoplasmic positivity with calcitonin

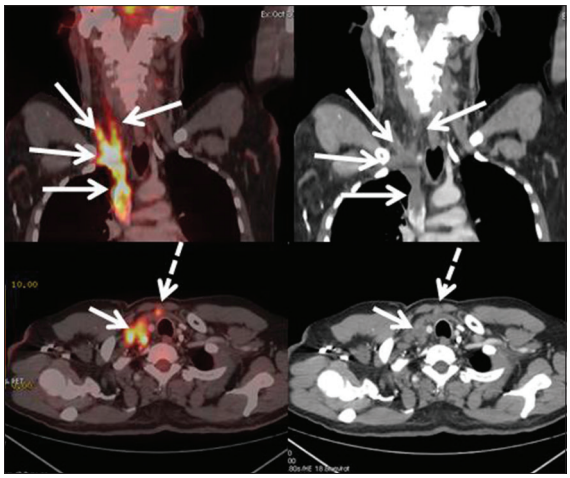

Figure 2: Coronal and axial section of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography showing intensely hypermetabolic hypo dense intraluminal filling defect right internal jugular vein, external jugular vein, subclavian vein confluencing at the right innominate vein with inferior extension into superior vena cava (arrow) and a small metabolically active pretracheal lymph node (dotted arrow)

neck revealed significantly shrunken thrombus in the right IJV with flow void and normal flow through the left innominate vein [Figure 4]. A contrast CT chest showed non-enhancing hypodense filling defect reduced in extent with tiny calcifications in the right IJV, EJV, subclavian veins suggesting chronic bland venous thrombus [Figure 5]. Serum calcitonin levels came down to 10 ng/L. A patient being disease free is on replacement therapy with thyroxine and on follow-up.

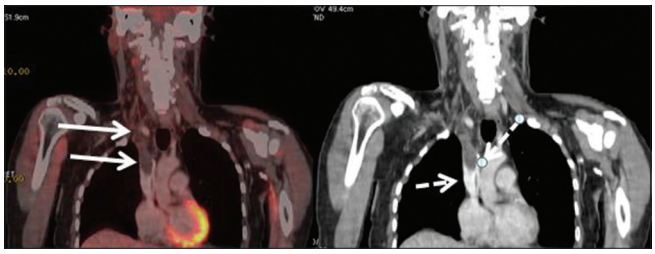

Figure 3: Coronal fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography postradiotherapy showing complete metabolic regression in the intravascular tumor (arrow) with significant reduction in the tumor thrombus load and better contrast passage through the superior vena cava (dotted arrow)

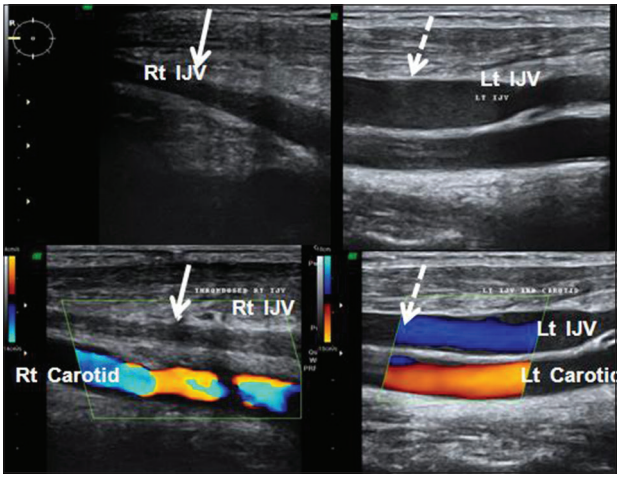

Figure 4: Color Doppler of the neck showing grossly shrunken thrombus in the right internal jugular vein with absent flow (arrow) and normal flow through the left innominate vein (dotted arrow)

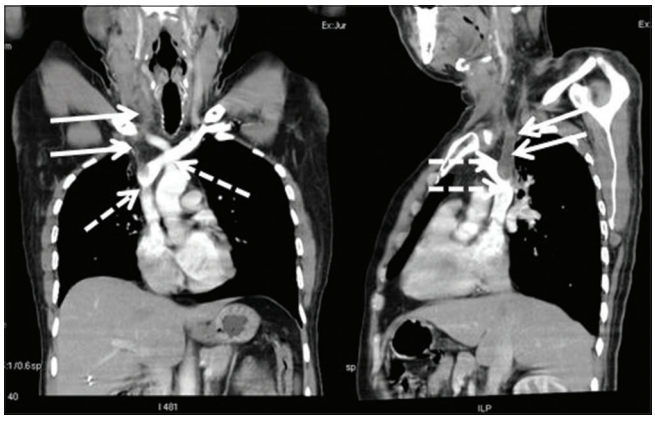

Figure 5: Coronal and sagittal contrast computed tomography chest showing hypodense filling defect in the right internal jugular vein reduced in extent with tiny calcifications, suggesting chronic thrombus (arrows), and patent left innominate vein filled with contrast streaking past the thrombus into superior vena cava (dotted arrows)

DISCUSSION

Medullary carcinoma of thyroid (MTC) is a tumor of parafollicular C-cells present in thyroid, which are derived from neural crest. MTC is known to produce its native hormone calcitonin. Melanotic variance is a rarity and also adds aggressiveness to the pathology.[1] Though the prognosis of a melanocytic variant of medullary carcinoma of thyroid is not known due to the scarcity of numbers it appears to be more aggressive.

Increased mitotic activity and cellular primitivity may contribute to bad prognosis.[2] On electron microscopic examination, the presence of both neurosecretory granules and melanosomes in the same tumor cells were demonstrated and suggested tumor arising from a common precursor cell with the potential for both melanocytic and C-cell differentiation.[3] Surgical excision by total thyroidectomy and local nodal clearance is the preferred treatment of choice. Because cancer often is multifocal, surgery includes total thyroidectomy with complete resection of nodes in the central compartment and an ipsilateral modified radical neck dissection if the patient presents with palpable lymph node disease.[4,5] The C-cells in medullary thyroid cancer do not concentrate iodine and are not part of the thyroid follicular apparatus; hence remnant ablation with high dose radioiodine is of no indication.[6] The effectiveness of external irradiation for medullary cancer is still controversial, but recent data indicate that it can be used in the curative treatment of patients with microscopic residual or gross disease.[7] The radiosensitivity of medullary cancer probably falls between that of differentiated cancers and anaplastic cancers.[8,9] Patients with detectable calcitonin concentrations after initial treatment and who have no other evidence of disease are followed up regularly.[10] Recurrence is usually local and nodal, however, metastasis to lungs, liver, and bones is known. Intravascular extension as tumoral thrombosis into major neck veins in papillary and follicular carcinoma thyroid though rare has been reported.[11] However, similar occurrence in medullary cancer has not yet been cited. Surgical intervention in the presence of SVC syndrome, however, remains controversial because of the treatment dilemma between perioperative morbidity and mortality with aggressive surgery and the poor prognosis with palliative therapy.[12] The preponderance of the tumoral thrombus predominantly in the right sided major neck veins is hypothesized by the migration of the tumor cells from the neck through the lymphatic channels in the right side of the neck draining through the right lymphatic duct also called the right thoracic duct which drains lymphatic fluid from the right thoracic cavity, the right arm, and from the right side of the neck and the head directly opening into the right subclavian IJV junction, unlike thoracic duct which opens at the left jugulo subclavian junction.[13] The presented clinical status was one of extensive tumoral thrombus with compromised venous lumens of the major right cervical veins. Patient's retrieval with an immediate hypofractionated IMRT approach not only salvaged the patient from impending SVC syndrome but also contained the tumor thrombus making it metabolically bland and regresses morphologically. F-18 FDG PET/CT outlined hypermetabolic

region inside the neck veins was principally taken as the guideline for carotid artery sparing IMRT planning of gross tumor volume and planning tumor volume. Hypofractionated schedule of 20 fraction 50 Gy instead of conventional 2 Gy, 25 fraction method was adapted.[8] This will reduce the treatment duration and also deliver higher dose per fraction with better therapeutic effect by overcoming radioresistance and achieving faster and better control of intravascular tumor load which was sanctified with gratifying clinical outcome.

CONCLUSION

The case had the distinction of more than year's record of events from the onset of disease, initial treatment, and the catastrophic tumor thrombus occurring 1 year later. PET/CT-aided diagnosis and radiotherapy planning with the rewarding response from a metabolically active tumor thrombus to a bland nontumoral thrombotic disease free status is the quintessence of this rare case.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Singh ZN, Ray R, Kumar N, Aron M, Gupta SD. Medullary thyroid carcinoma with melanin production – A case report. Indian J Pathol Microbiol 1999;42:159-63.
2. Singh K, Sharma MC, Jain D, Kumar R. Melanotic medullary carcinoma of thyroid – Report of a rare case with brief review of literature. Diagn Pathol 2008;3:2.
3. Uribe M, Fenoglio-Preiser CM, Grimes M, Feind C. Medullary carcinoma of the thyroid gland. Clinical, pathological, and immunohistochemical features with review of the literature. Am J Surg Pathol 1985;9:577-94.
4. Moley JF, Debenedetti MK, Dilley WG, Tisell LE, Wells SA. Surgical management of patients with persistent or recurrent medullary thyroid cancer. J Intern Med 1998;243:521-6.
5. Evans DB, Fleming JB, Lee JE, Cote G, Gagel RF. The surgical treatment of medullary thyroid carcinoma. Semin Surg Oncol 1999;16:50-63.
6. American Thyroid Association Guidelines Task Force, Kloos RT, Eng C, Evans DB, Francis GL, Gagel RF, *et al*. Medullary thyroid cancer: Management guidelines of the American Thyroid Association. Thyroid 2009;19:565-612.
7. Greenfield LD, Ucmakli A, George FW 3rd. The role of radiation therapy in the treatment of medullary thyroid cancer. Contemp Surg 1981;18:59.
8. Simpson W, Sutcliffe S, Gospodarowicz M. The thyroid. In: Moss W, Cox J, editors. Radiation Oncology: Rationale, Technique, Results. St. Louis: CV Mosby; 1989.
9. Tubiana M, Haddad E, Schlumberger M, Hill C, Rougier P, Sarrazin D. External radiotherapy in thyroid cancers. Cancer 1985;55 9 Suppl: 2062-71.
10. Stepanas AV, Samaan NA, Hill CS Jr, Hickey RC. Medullary thyroid carcinoma: Importance of serial serum calcitonin measurement. Cancer 1979;43:825-37.
11. Patel PC, Millman B, Pellitteri PK, Woods EL. Papillary thyroid carcinoma presenting with massive angioinvasion of the great vessels of the neck and chest. Otolaryngol Head Neck Surg 1997;117:S117-20.
12. Wiseman O, Preston PG, Clarke JM. Presentation of thyroid carcinoma as a thrombosed external jugular vein, with intraluminal tumour thrombus in the great veins. Eur J Surg Oncol 2000;26:816-7.
13. Drake RC, Vagl AW, Mitchell AW, editors. The Body, Grays Anatomy for Students. 2nd ed., Ch. 1. Elsevier: Churchill Livingstone; 2010. p. 33.