A Rare Case of Synchronous Papillary Microcarcinoma and Metastatic Neuroendocrine Tumor of Unknown Primary

Abstract

Thyroid papillary microcarcinomas (PMCs) usually follow a very benign clinical course and are rarely metastatic. Any case of PMC presenting with distant metastases without any rising thyroglobulin level should be suspected to have any other primary apart from the thyroid and a meticulous clinical and diagnostic approach should be considered to identify the second primary. We hereby present a case of 52-year-old female treated as PMC with metastatic liver lesion, which was initially thought to be of thyroidal origin. Later, it was diagnosed as a metastatic neuroendocrine tumor of unknown primary.

Keywords: *Neuroendocrine tumor, papillary microcarcinoma, thyroglobulin*

Shambo Guha Roy, Sarthak Tripathy, Girish Kumar Parida, Shipra Agarwal[1], Chandrasekhar Bal

Departments of Nuclear Medicine and [1]Pathology, All India Institute of Medical Sciences, New Delhi, India

Case report

Here, we present a case of 52-year-old female who was referred to our thyroid clinic 1 year after she underwent total thyroidectomy (TT) for solitary thyroid nodule which was Bethesda category VI on fine-needle aspiration cytology (FNAC). Later histopathology showed it to be papillary microcarcinoma of size 8 mm. Six months following her surgery, she started complaining of anorexia, fatigue, and right hypochondriac pain. An ultrasound abdomen revealed multiple hypoechoic liver lesions, which were suspicious for metastases. In the next 6 months, she also underwent a contrast-enhanced computed tomography (CECT) and fluorodeoxyglucose-positron emission tomography-computed tomography (FDG-PET-CT) for the evaluation of the liver lesion. CECT revealed large hypodense enhancing lesion involving the right lobe of the liver and FDG-PET-CT showed them to be hypermetabolic, suggesting to be of a metastatic disease [Figure 1a-c]. She then underwent FNAC from the liver lesion which was reported as metastatic carcinoma. In view of a known thyroid malignancy, the primary clinician attributed the metastasis to be of thyroid origin and referred the patient to our center for radioiodine therapy. As per our institute protocol, 4 weeks off thyroxine, 100 mCi of empirical 131-I therapy was planned considering the possibility of non-thyroglobulin (Tg) secreting metastasis as serum Tg was <2 ng/ml. However, the posttherapy I-131 whole body scan did not show any abnormal concentration in the liver [Figure 2a and b; anterior and posterior images, respectively]. In view of normal Tg, nonradioiodine concentrating liver lesion and history of micropapillary carcinoma, which is rarely metastatic, possibility of second malignancy was considered. To confirm the diagnosis, a repeat liver biopsy was planned at our institute. The histopathology revealed neuroendocrine tumor (NET) cells [Figure 3a and b] which were immunopositive for chromogranin and synaptophysin [Figure 3c and d, respectively]. MIB-1 index could not be assessed due to tiny nature of the biopsy. Later, her serum chromogranin level was found to be >650 ng/l. Subsequently, a 68-Ga-DOTANOC PET-CT was planned which showed somatostatin receptor expressing tumor in both lobes of the liver with extensive skeletal metastasis [Figure 4a-c; transaxial CT, PET-CT, and maximum intensity projection images, respectively]. Here, DOTANOC PET-CT detected skeletal metastasis which was not detected previously. In spite of both FDG and DOTANOC PET-CT,

How to cite this article: Roy SG, Tripathy S, Parida GK, Aggrawal S, Bal C. A rare case of synchronous papillary microcarcinoma and metastatic neuroendocrine tumor of unknown primary. Indian J Nucl Med 2017;32:59-61.

Address for correspondence:
Prof. Chandrasekhar Bal, Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi - 110 029, India.
E-mail: csbal@hotmail.com

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.IJNM_58_17

Quick Response Code:

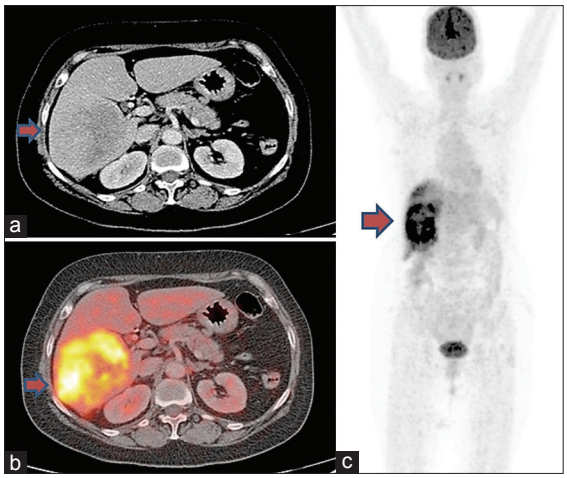

Figure 1: Fluorodeoxyglucose-positron emission tomography-computed tomography shows large hypodense, enhancing, hypermetabolic lesion involving the right lobe of liver, suggesting metastatic disease (a-c; transaxial computed,tomography, positron emission tomography-computed tomography and maximum intensity projection images, respectively)

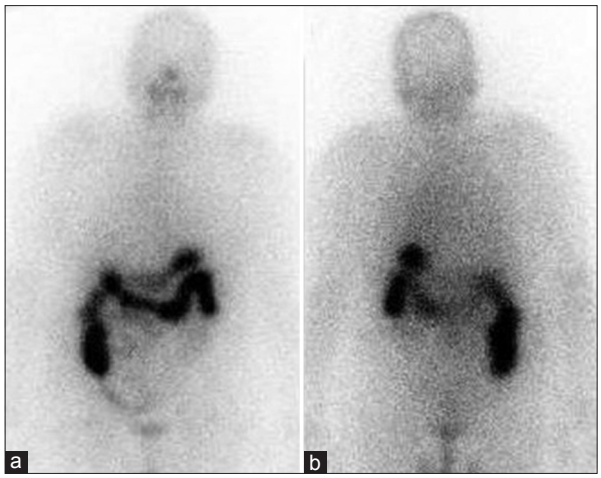

Figure 2: No abnormal rejection activity index accumulation noted in liver (a and b; anterior and posterior images, respectively)

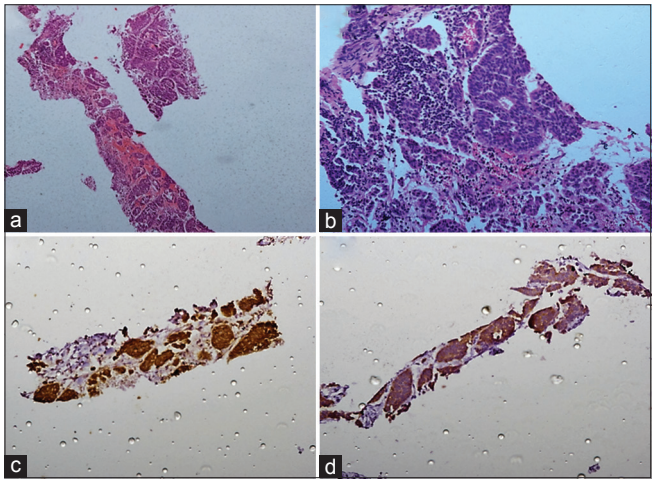

Figure 3: The histopathology reveals neuroendocrine tumor cells (a and b), immunopositive for chromogranin and synaptophysin (c and d, respectively)

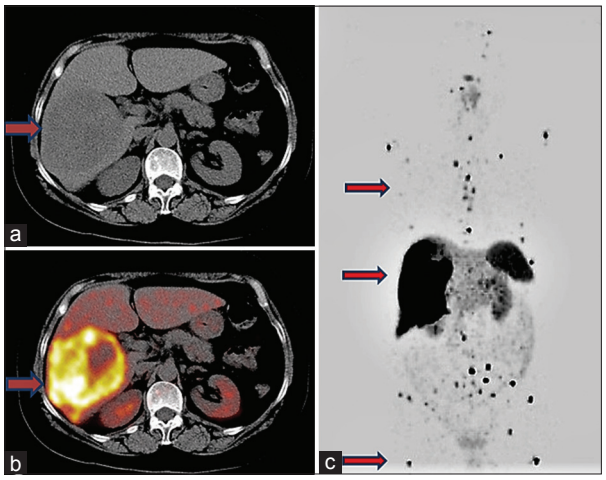

Figure 4: 68-Ga-DOTANOC positron emission tomography-computed tomography shows somatostatin receptor expressing tumor in both lobes of liver with extensive skeletal metastasis (a-c; transaxial computed tomography, positron emission tomography-computed tomography and maximum intensity projection images, respectively)

primary tumor remained undetected. In view of extensive metastatic disease, she was put on long-acting octreotide and planned for 177-Lutetium DOTATATE therapy.

Discussion

Thyroid papillary microcarcinomas (PMCs) are defined as tumors <1 cm in greatest diameter. Papillary variety accounts for the majority of microcarcinomas followed by the follicular type. PMCs show a very benign natural history. Distant metastases are found in only 0.37% of cases as reported by Roti *et al*.[1] Metastases to cervical lymph nodes and other distant organs occur more often in nonincidental PMC than in incidental ones.[2] However, nonincidental PMC have a much more aggressive course as compared to the incidental ones, and TT with central lymph node dissection is recommended.[3]

Cervical lymph nodes, lung, and bone are the most common sites of metastasis from differentiated carcinoma thyroid (DTC). Metastases to other organs are infrequent. Liver metastasis is rare in DTC. There are only few case reports and one case series published.[4-7] In our patient, the liver lesion was attributed initially to metastasis from thyroid cancer. Due to the rarity of liver metastases in DTC, especially in a setting of microcarcinoma with normal Tg, a second malignancy was also kept as other differential diagnosis. As FDG-PET/CT could not locate any other primary, a core liver biopsy was planned, which showed it to be metastatic NET.

This case presented is an example of synchronous double primary, i.e., the second malignancy occurred within 6 months of the primary malignancy.[8] Thyroid carcinoma is known to be associated to with second malignancies.[9-11] The reported incidence of synchronous or metachronous

nonthyroidal malignancies is 13.9%.[11] Leukemia, breast, and colon cancers have been reported to have higher incidence in thyroid cancer survivor.[9,10] We could find only one report of neuroendocrine tumor as synchronous second malignancy with DTC.[11]

Based on the length of the time of tumor diagnoses, dual malignancies can be divided into two categories, i.e., synchronous and metachronous.[12] The cause of multiple primary cancers is still an enigma but much of the cause can be attributed to the family history, immunologic and genetic defects, prolonged exposure to carcinogens, chemotherapy, and radiotherapy to the primary cancer and field cancerization.[13,14] In literature, Noh *et al*. have also reported a case of a quadruple cancer involving synchronous ovarian and endometrial cancer that occurred after breast and rectal cancer.[13] The diagnostic criterion for multiple primary malignancies was laid down by Warren and Gates way back in 1932.[15] The salient features included that (a) each cancer must be definitively malignant by histopathology, (b) they must be histologically different, and (c) the possibility of metastasis among the cancers must be excluded. Since it was not very easy to differentiate between multiple primaries and multicentric cancers with this criterion, Moertel suggested another criterion which is widely used today.[8] According to this criterion, multiple malignancies are classified in three groups – (1) multiple primary malignant neoplasms of multicentric origin, (2) multiple primary malignant neoplasms of different tissues or organs, and (3) combination of the above two.

This case presents a synchronous DTC with neuroendocrine tumor of unknown primary. After extensive literature review, we could found only one reported such case.[11] It also highlights the importance of the meticulous unbiased clinical workup while dealing with a low-grade neoplasm with normal serum tumor markers, to name it as a metastatic disease. Our patient had papillary microcarcinoma which is rarely metastatic. Second, liver metastases are rare from DTC and her serum Tg levels were <2 ng/ml. All these points suggested the liver lesion unlikely to be of thyroidal origin. Hence, we suggest any suspicious liver lesion should be evaluated histopathologically in case DTC, unless it shows radioiodine concentration.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Roti E, degli Uberti EC, Bondanelli M, Braverman LE. Thyroid papillary microcarcinoma: A descriptive and meta-analysis study. Eur J Endocrinol 2008;159:659-73.
2. Roti E, Rossi R, Trasforini G, Bertelli F, Ambrosio MR, Busutti L, *et al.* Clinical and histological characteristics of papillary thyroid microcarcinoma: Results of a retrospective study in 243 patients. J Clin Endocrinol Metab 2006;91:2171-8.
3. Karatzas T, Vasileiadis I, Kapetanakis S, Karakostas E, Chrousos G, Kouraklis G. Risk factors contributing to the difference in prognosis for papillary versus micropapillary thyroid carcinoma. Am J Surg 2013;206:586-93.
4. Brient C, Mucci S, Taïeb D, Mathonnet M, Menegaux F, Mirallié E, *et al.* Differentiated thyroid cancer with liver metastases: Lessons learned from managing a series of 14 patients. Int Surg 2015;100:490-6.
5. Song HJ, Xue YL, Xu YH, Qiu ZL, Luo QY. Rare metastases of differentiated thyroid carcinoma: Pictorial review. Endocr Relat Cancer 2011;18:R165-74.
6. Djenic B, Duick D, Newell JO, Demeure MJ. Solitary liver metastasis from follicular variant papillary thyroid carcinoma: A case report and literature review. Int J Surg Case Rep 2015;6C:146-9.
7. Kamaleshwaran KK, Natarajan S, Mohanan V, Shinto AS. Unusual case of hepatic metastasis in follicular thyroid carcinoma detected using I-131 whole body scintigraphy and single-photon emission computerized tomography/computerized tomography. Indian J Nucl Med 2015;30:358-9.
8. Moertel CG. Multiple primary malignant neoplasms: Historical perspectives. Cancer 1977;40 4 Suppl:1786-92.
9. Subramanian S, Goldstein DP, Parlea L, Thabane L, Ezzat S, Ibrahim-Zada I, *et al.* Second primary malignancy risk in thyroid cancer survivors: A systematic review and meta-analysis. Thyroid 2007;17:1277-88.
10. Rubino C, de Vathaire F, Dottorini ME, Hall P, Schvartz C, Couette JE, *et al.* Second primary malignancies in thyroid cancer patients. Br J Cancer 2003;89:1638-44.
11. Murray SE, Schneider DF, Bauer PS, Sippel RS, Chen H. Synchronous and antecedent nonthyroidal malignancies in patients with papillary thyroid carcinoma. J Am Coll Surg 2013;216:1174-80.
12. Suzuki T, Takahashi H, Yao K, Inagi K, Nakayama M, Makoshi T, *et al.* Multiple primary malignancies in the head and neck: A clinical review of 121 patients. Acta Otolaryngol Suppl 2002;547:88-92.
13. Noh SK, Yoon JY, Ryoo UN, Choi CH, Sung CO, Kim TJ, *et al.* A case report of quadruple cancer in a single patient including the breast, rectum, ovary, and endometrium. J Gynecol Oncol 2008;19:265-9.
14. Slaughter DP, Southwick HW, Smejkal W. Field cancerization in oral stratified squamous epithelium; clinical implications of multicentric origin. Cancer 1953;6:963-8.
15. Warren S, Gates O. Multiple primary malignant tumors: A survey of the literature and statistical study. Am J Cancer 1932;16:1358-414.