Acta Clin Croat 2023; 62:230-233
doi: 10.20471/acc.2023.62.01.27

Case Report

SIMULTANEOUS METASTASES OF PAPILLARY THYROID CARCINOMA AND NEUROENDOCRINE TUMOR OF THE CECUM TO CERVICAL LYMPH NODES: A CASE REPORT

Matija Romić[1], Ivan Blažeković[1], Neven Mateša[2], Maja Franceschi[1], Ines Šiško-Markoš[1], Zvonko Kusić[3], Ana Fröbe[1,4] and Tomislav Jukić[1,5]

[1]Department of Oncology and Nuclear Medicine, Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[2]Department of Pathology and Cytology, Sestre milosrdnice University Hospital Center, Zagreb, Croatia;
[3]Croatian Academy of Sciences and Arts, Zagreb, Croatia;
[4]School of Dental Medicine, University of Zagreb, Zagreb, Croatia
[5]School of Medicine, University of Zagreb, Zagreb, Croatia

SUMMARY – We present a case of a patient with simultaneous cervical lymph node metastasis of papillary thyroid cancer (PTC) and cecum neuroendocrine tumor (NET). A 45-year-old male patient with the diagnosis of metastatic NET of the cecum underwent fine needle aspiration (FNA) of a positron emission tomography with 18F-fluorodeoxyglucose (18F-FDG PET) positive nodule in the left thyroid lobe. Due to FNA finding suspect of PTC, the patient underwent total thyroidectomy with central neck dissection. Histopathologic finding revealed PTC of the left thyroid lobe and small solitary lymph node PTC metastasis in the central neck region. Postoperative evaluation with neck ultrasound (US) revealed two enlarged suspected lymph nodes in cervical regions III and IV on the left side of the neck and the patient underwent FNA with measurement of thyroglobulin (Tg) in the aspirates. The FNA finding of the cervical lymph node in the region III revealed PTC metastasis with high Tg value in the aspirate, while FNA finding of the cervical lymph node in the region IV revealed NET metastasis with low Tg value in the aspirate. Postoperative serum Tg value was 17.75 μg/L and the patient underwent 5550 MBq iodine-131 (I-131) therapy. A year after I-131 therapy, follow-up neck US demonstrated complete cure of PTC cervical lymph node metastasis in the region III and stable in size NET cervical lymph node metastasis in the region IV. To our knowledge, this is the first report of simultaneous occurrence of cervical lymph node metastases of PTC and NET of the cecum.

Key words: *Papillary thyroid cancer; Neuroendocrine tumor; Cervical lymph node; Metastasis*

Introduction

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy, showing a significant increase in the incidence in the last few decades[1], mainly due to improved diagnostics. The vast majority of this increase can be attributed to the increase in the incidence of papillary thyroid cancer (PTC) due to widespread use of ultrasound (US) and fine needle aspiration biopsy (FNA) of small thyroid nodules as part of cancer screening programs[2,3]. Around 5% of thyroid nodules are malignant. The use of positron emission tomography with ^{18}F-fluorodeoxyglucose (^{18}F-FDG PET) has led to an increased number of newly detected thyroid lesions in 1%-2% of patients[4].

Correspondence to: Prof. Tomislav Jukić, MD, PhD, Department of Oncology and Nuclear Medicine, Sestre milosrdnice University Hospital Center, Vinogradska c. 29, HR-10000 Zagreb, Croatia
E-mail: tomislav.jukic@kbcsm.hr

Received February 16, 2021, accepted May 11, 2021

Approximately 35% of ^{18}F-FDG PET positive thyroid nodules proved to be cancerous[5]. Neuroendocrine tumors (NETs) are a group of rare tumors that arise from neuroendocrine cells throughout the body. They account for 0.46% of gastroenteropancreatic and bronchopulmonary malignancies[6]. Colorectal NETs (CRNETs) are the second most common NETs in the gastrointestinal tract with the incidence of 0.3-1 *per* 100,000[7] and the incidence has increased in the last few decades[8]. Improvement and increased use of endoscopic diagnostics, computed tomography (CT), magnetic resonance imaging (MRI), US, nuclear medicine diagnostic procedures and advances in histologic diagnosis have contributed to the increased incidence of NETs. Up to 34.5% to 48% of all colorectal carcinoids occur in the cecum and ascending colon[9]. More than 40% of cecal tumors have distant metastatic disease at diagnosis[10]. PTC metastases in cervical lymph nodes are frequent[11-13], however, NET cervical lymph node metastases are rare[14]. We present a patient with simultaneous cervical lymph node metastasis of PTC and NET of the intestinal tract.

Case Report

A 45-year-old male patient underwent CT of the abdomen due to progression of diarrhea and abdominal cramps, as well as condition deterioration with weight loss. In January 2017, due to CT finding of tumor mass in the area of ileocecal valve with threatening development of ileus, right-sided hemicolectomy was performed. Histopathologic finding revealed a grade 2 neuroendocrine tumor, macroscopically 5 cm in size, located on the Bauchini valve, with infiltration of all wall layers and perforation of serosa, positive for chromogranin and synaptophysin. A total of 6 of 21 lymph nodes were infiltrated by tumor with lymphovascular and perineural invasion. Postoperative examination with somatostatin receptor scintigraphy (Octreoscan), as well as further diagnostic procedures revealed no pathology suggestive of distant spread. In May 2019, the patient underwent follow-up Octreoscan. A solitary focus of pathological accumulation in the right liver lobe, as well as faint pathological accumulation of the radiopharmaceutical in the right iliac bone was reported, suggestive of somatostatin receptor expression. MRI of the abdomen and pelvis revealed focal lesions of the liver in segments VI and VIII, measuring 18 mm and 11 mm in diameter, respectively, as well as a few smaller liver lesions, indicating dissemination of the underlying disease. The patient started taking Sandostatin LAR therapy, together with short-acting Sandostatin. In August 2019, prior to treatment of liver metastases, ^{18}F-FDG PET/CT was performed. NET liver metastases were FDG negative but intense focal ^{18}F-FDG accumulation in the left thyroid lobe was reported (SUV max=6.6) (Fig. 1) and FNA of

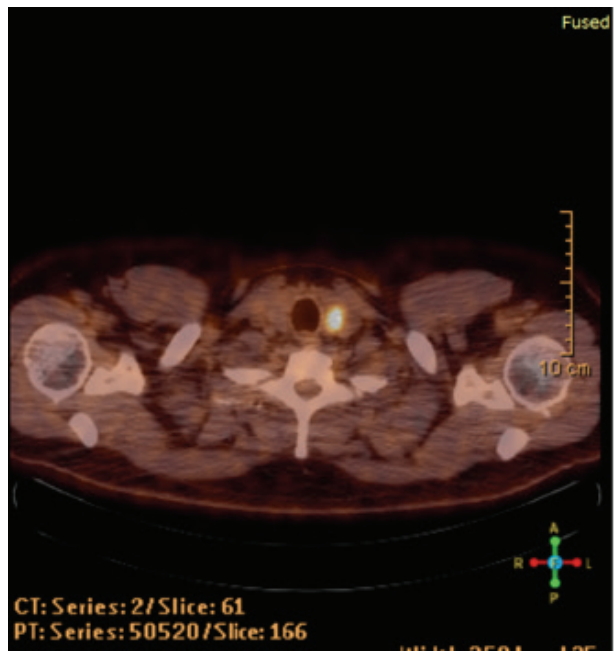

Fig. 1. Positron emission tomography-computed tomography with ^{18}F fluorodeoxyglucose (^{18}F-FDG PET/CT): intense focal ^{18}F- FDG accumulation in the left thyroid lobe (SUV max=6.6).

the left thyroid lobe nodule was performed. The FNA finding was suspicious of papillary thyroid carcinoma. A decision was made to perform total thyroidectomy first and then ablation of NET liver metastases. In October 2019, the patient underwent total thyroidectomy with central neck dissection. Histopathologic finding revealed PTC of the left thyroid lobe measuring 1 cm in diameter without extrathyroidal extension, and small solitary lymph node PTC metastasis in central neck region measuring 2 mm in diameter (TNM stage pT1aN1aMx). In December 2019, postoperative oncologic evaluation of PTC demonstrated high postoperative serum stimulated Tg level of 17.75 μg/L. Neck US described a suspected lymph node measuring 8 mm in diameter on the left side of the neck in the cer-

vical region III and a suspected lymph node measuring 10 mm in diameter in the cervical region IV. The FNA finding of the lymph node in the cervical region III described clusters of atypical epithelial cells with locally expressed intranuclear cytoplasmic inclusions and high Tg value in the aspirate, revealing metastasis of PTC (Fig. 2). However, FNA finding of the lymph node in the cervical region IV described peripheral blood cells, lymphocytes, and small- to medium-sized clusters of densely packed small atypical cells with negative Tg in the aspirate revealing NET metastasis (Fig. 3). Octreoscan and PET/CT performed earlier did not report pathologic accumulation of radiopharmaceuticals in the neck regions. The patient was treated with 5550 MBq of I-131. Posttreatment whole body scan with I-131 revealed accumulation of I-131 in the thyroid bed. However, there was no pathologic accumulation of I-131 in the left lateral neck region. The patient was under follow-up on Sandostatin LAR therapy and in January 2020 underwent CT guided microwave ablation of the NET liver metastases. A year after I-131 therapy, follow-up neck US reported stable in size NET cervical lymph node metastasis in region IV. However, PTC cervical lymph node metastasis in region III was not reported, probably due to positive treatment response to I-131 therapy with low serum Tg level.

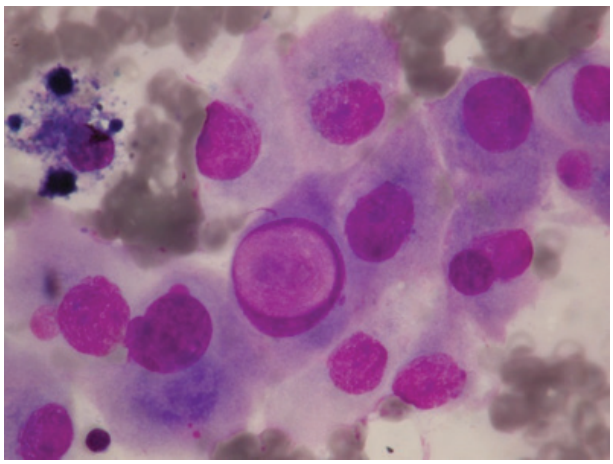

Fig. 2. Lymph node metastasis of papillary thyroid cancer. Atypical epithelial cells with locally expressed intranuclear cytoplasmic inclusions (MGG x1000).

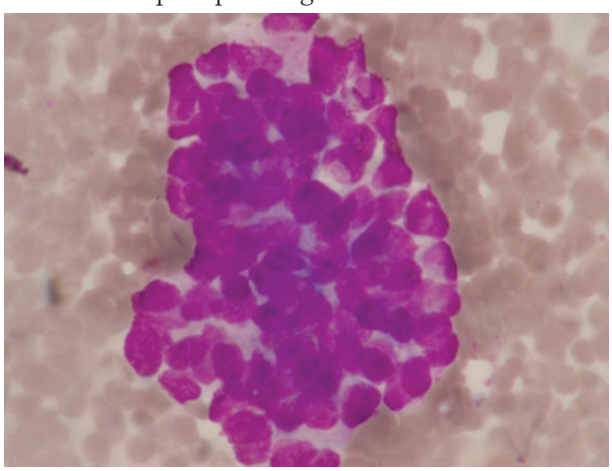

Fig. 3. Neuroendocrine tumor lymph node metastasis. Cluster of densely packed small atypical cells (MGG x400).

Conclusion

Concomitant occurrence of other malignant conditions together with gastrointestinal NETs has already been described in the literature with increased incidence of second primary malignancies in patients with carcinoid tumors[15]. Regional lymph nodes are the most common location of CRNET metastases[16]. However, cervical and upper mediastinal lymph node metastases from gastrointestinal and pancreatic NETs are rare and have been reported in less than 8.7% of patients[14]. Furthermore, simultaneous metastases of PTC and NET of the intestinal tract to cervical lymph nodes are very rare and have been reported only once in the literature[17]. The patient presented had simultaneous cervical lymph node metastasis of PTC and NET of small intestine, which is more common than CRNET[17]. Our case report is therefore the first presentation of a patient with concomitant CRNET and PTC metastasis in the cervical lymph node group.

Acknowledgment

This work was supported by the Croatian Science Foundation project entitled Genetic and Epigenetic Markers as Indicators of Aggressiveness of Differentiated Thyroid Cancer (IP-2019-04-1130).

References

1. Noone AM, Howlader N, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA, editors. SEER Cancer Statistics Review, 1975-2015, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2015/, based on November 2017 SEER data submission, posted to the SEER web site, April 2018.

2. Staničić J, Prpić M, Jukić T, Borić M, Kusić Z. Thyroid nodularity – true epidemic or improved diagnostics. Acta Clin Croat. 2009;48:413-8.
3. Li N, Du XL, Reitzel LR, Xu L, Sturgis EM. Impact of enhanced detection on the increase in thyroid cancer incidence in the United States: review of incidence trends by socioeconomic status within the surveillance, epidemiology, and end results registry, 1980-2008. Thyroid. 2013;23:103-10. doi: 10.1089/thy.2012.0392
4. Croatian Institute for Public Health. Croatian National Cancer Registry. Cancer incidence in Croatia 2014. Bulletin No. 29, Zagreb, 2016.
5. Soelberg KK, Bonnema SJ, Brix TH, Hegedüs L. Risk of malignancy in thyroid incidentalomas detected by 18F-fluorodeoxyglucose positron emission tomography: a systematic review. Thyroid. 2012;22(9):918-25. doi: 10.1089/thy.2012.0005
6. Hallet J, Law CH, Cukier M, Saskin R, Liu N, Singh S. Exploring the rising incidence of neuroendocrine tumors: a population-based analysis of epidemiology, metastatic presentation, and outcomes. Cancer. 2015;121(4):589-97. doi: 10.1002/cncr.29099
7. Amin MB, Greene FL, Edge SB, *et al*. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93-9. doi: 10.3322/caac.21388
8. Dasari A, Shen C, Halperin D, *et al*. Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. JAMA Oncol. 2017;3(10):1335-42. doi: 10.1001/jamaoncol.2017.0589
9. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer. 2003;97(4):934-59. doi: 10.1002/cncr.11105
10. Mandair D, Caplin ME. Colonic and rectal NET's. Best Pract Res Clin Gastroenterol. 2012;26(6):775-89. doi: 10.1016/j.bpg.2013.01.007
11. Nam-Goong IS, Kim HY, Gong G, *et al*. Ultrasonography-guided fine-needle aspiration of thyroid incidentaloma: correlation with pathological findings. Clin Endocrinol (Oxf). 2004;60(1):21-8. doi: 10.1046/j.1365-2265.2003.01912.x
12. Grebe SK, Hay ID. Thyroid cancer nodal metastases: biologic significance and therapeutic considerations. Surg Oncol Clin North Am. 1996;5(1):43-63.
13. Haugen BR, Alexander EK, Bible KC, *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 Jan;26(1):1-133. doi: 10.1089/thy.2015.0020
14. Wang YZ, Mayhall G, Anthony LB, Campeau RJ, Boudreaux JP, Woltering EA. Cervical and upper mediastinal lymph node metastasis from gastrointestinal and pancreatic neuroendocrine tumors: true incidence and management. J Am Coll Surg. 2012;214(6):1017-22. doi: 10.1016/j.jamcollsurg.2012.02.006
15. Rivadeneira D, Tuckson W, Naab T. Increased incidence of second primary malignancy in patients with carcinoid tumors: case report and literature review. J Natl Med Assoc. 1996;88:310-2.
16. Fields AC, McCarty JC, Lu P, *et al*. Colon neuroendocrine tumors: a new lymph node staging classification. Ann Surg Oncol. 2019;26(7):2028-36. doi: 10.1245/s10434-019-07327-6
17. Markou KD, Goudakos JK, Triaridis S, Televantou D, Hytiroglou P, Nikolaou A. Simultaneous metastatic papillary thyroid carcinoma and carcinoid of the small intestine in the cervical lymph node group. Thyroid. 2010;20(9):1025-8. doi: 10.1089/thy.2009.0438

Sažetak

ISTODOBNO PRISUTNE PRESADNICE PAPILARNOG KARCINOMA ŠTITNJAČE I NEUROENDOKRINOG TUMORA CEKUMA U LIMFNIM ČVOROVIMA VRATA: PRIKAZ SLUČAJA

M. Romić, I. Blažeković, N. Mateša, M. Franceschi, I. Šiško-Markoš, Z. Kusić, A. Fröbe i *T. Jukić*

Prikazujemo slučaj istodobno prisutne presadnice papilarnog karcinoma štitnjače (PTC) i neuroendokrinog tumora (NET) cekuma u limfnim čvorovima vrata. Bolesniku u dobi 45 godina s dijagnozom metastatskog NET-a cekuma učinjena je apsiracijska biopsija tankom iglom (FNA) čvora u lijevom režnju štitnjače pozitivnog na pozitronskoj emisijskoj tomografiji s ^{18}F-fluorodeoksiglukozom (^{18}F-FDG PET). Zbog postavljene sumnje na PTC, a temeljem nalaza FNA, bolesniku je učinjena totalna tireoidektomija s centralnom disekcijom vrata. Patohistološki nalaz potvrdio je PTC u lijevom režnju štitnjače i solitarnu presadnicu PTC-a u malom limfnom čvoru u centralnoj regiji vrata. Poslijeoperacijskom obradom ultrazvučno (UZV) su na lijevoj strani vrata u regijama III. i IV. otkrivena dva povećana suspektna limfna čvora te je bolesniku učinjena FNA s određivanjem tireoglobulina (Tg) u aspiratima. Nalaz FNA limfnog čvora u regiji III. odgovarao je presadnici PTC-a uz visoku vrijednost Tg-a u aspiratu, dok je nalaz FNA limfnog čvora u regiji IV. odgovarao presadnici NET-a uz nisku vrijednost Tg-a u aspiratu. Poslijeoperacijska vrijednost Tg-a u serumu bila je 17,75 μg/L te je bolesnik primio terapiju jodom-131 (I-131) aktiviteta 5550 MBq. Godinu dana nakon terapije I-131 kontrolni UZV vrata pokazao je potpunu regresiju presadnice PTC-a u regiji III. i stacionaran nalaz presadnice NET-a u regiji IV. Prema našim saznanjima, ovo je prvi prikaz slučaja istodobno prisutne presadnice PTC-a i NET-a cekuma u limfnim čvorovima vrata.

Ključne riječi: *Papilarni karcinom štitnjače; Neuroendokrini tumor; Limfni čvor vrata; Presadnica*