SYNCHRONOUS NECK MELANOMA AND PAPILLARY THYROID CANCER: A CASE REPORT

Vladimir Pantelic¹, Sasa Zunjic¹, Dusan Ruzicic¹, Ivan Radosaljevic², Ivan Paunovic³ and Vladan Zivaljevic³

¹Department of Surgery, General Hospital Valjevo, Serbia

²Department of Surgery, Faculty of Medical Sciences, University of Kragujevac, Serbia

³Center for Endocrine Surgery, Institute of Endocrinology, Diabetes and Diseases of Metabolism, Clinical Center of Serbia, Belgrade, Serbia

ISTOVREMENI MALIGNI MELANOM VRATA I PAPILARNI KARCINOM ŠTITNE ŽLEZDE: PRIKAZ SLUČAJA

Vladimir Pantelić¹, Saša Žunjić¹, Dušan Ružičić¹, Ivan Radosaljević², Ivan Paunović³ i Vladan Živaljević³

¹Odeljenje za hirurgiju, Opšta bolnica Valjevo, Srbija

²Katedra za hirurgiju, Fakultet medicinskih nauka, Univerzitet u Kragujevcu, Srbija

³Centar za endokrinu hirurgiju, Institut za endokrinologiju, dijabetes i bolesti metabolizma, Klinički centar Srbije, Beograd, Srbija

Received/Primljen: 05.01.2021.

Accepted/Prihvaćen: 02.03.2021.

ABSTRACT

Introduction: The synchronous malignant melanoma of the neck and papillary thyroid cancer is rare but severe condition. Here, we describe the case of a patient with papillary thyroid cancer and melanoma invasivum cutis. **Case report:** A 49-year-old man had a change on the neck at the last 3-4 months that he accidentally noticed. He had hoarse voice, was afebrile, did not sweat more than usual and feel exhausted, without rash or itching. MR examination of the neck and upper mediastinum before the surgery indicated a hyperintense focal change in the left thyroid gland which dimensions was 19 x 15 mm and several hyperintense inhomogeneous lymph glands of the jugular chain, on the both sides, with different sizes. On the basis of the conducted analyzes, in addition to total thyroidectomy, two-sided functional dissection of the lymph nodes of the neck was performed. The pathohistological diagnosis of the left lobus was: Carcinoma papillary glandulae thyreoideae invasivum (G-I, nG-I, pT2, Lx, Vo). CT of head, neck and thorax were made, where it was noticed that the CT of the head and lungs were normal. PET/CT findings indicated that there was no rest or recurrence of the tumor. **Conclusion:** The message from this case report is that when diagnosing and treating thyroid cancer, the observed changes in the neck lymph nodes also indicate cancers of non-thyroid pathology such as malignant melanoma.

Keywords: papillary thyroid cancer, malignant melanoma, lymph nodes.

SAŽETAK

Uvod: Sinhroni maligni melanoma vrata i papilarni karcinom štitne žlezde je retko i opasno stanje. Ovde opisujemo slučaj pacijenta sa papilarnim karcinomom štitne žlezde i malignim melanomom vrata. **Prikaz slučaja:** Muškarac star 49 godina je imao promenu na vratu u poslednja 3-4 meseca koju je slučajno primetio i mislio je da se lako uvećava. Poslednjih dana je imao hrapav glas, bez temperature, nije se znojio više nego obično, iscrpljenost nije bila prisutna. MR pregled vrata i gornjeg medijastinuma je ukazivala na hiperintenznu fokalnu promenu leve štitne žlezde dimenzija 19 x 15 mm i uvećane limfne čvorove jugularnog lanca obotranu, različitih dimenzija. Na osnovu sprovedenih analiza, intraoperativno je odlučeno da se pored totalne tireoidektomije izvrši i dvostrana funkcionalna disekcija limfnih čvorova vrata. Patohistološka dijagnoza levog lobusa je bila sledeća: Carcinoma papillari glandulae thireoideae invasivum (G-I, nG-I, pT2, Lx, Vo). Napravljeni su CT glave, vrata i grudnog koša, gde je uočeno da su CT glave i pluća normalni. Nalazi PET/CT ukazivali su na to da tumorske rezidue ne postoje. **Zaključak:** Poruka iz ovog prikaza slučaja je da prilikom dijagnostikovanja i tretiranja karcinoma štitne žlezde uočene promene u limfnim čvorovima vrata ukazuju i na kancere netiroidne patologije kao što je maligni melanom.

Ključne reči: papilarni karcinom štitne žlezde, maligni melanom, limfni čvorovi.

INTRODUCTION

Worldwide malignant melanoma is the commonest tumor of the skin, though it occurs in many other organs. Malignant melanoma is a skin cancer that is caused by the malignant transformation of melanocytes. Melanocytes are neural crest-derived cells that migrate to the skin, mucous membranes and several other sites. The incidence of melanoma has been steadily increasing in the past several decades with an annual increase of 3-8% worldwide (1). Most common form of melanoma are the cutaneous and the ocular form. It occurs slightly more often in males 2.8:1 male to female ratio and the age range is from 20-83 years with an average age of 56 years (2). Malignant melanoma can be successfully treated if it is detected in the early stages of development. Surgery is the standard treatment for early stage melanoma. However, the prognosis associated with advanced-stage malignant melanoma is poor; the disease accounts for ~4% of all skin cancers, but results in 80% of skin cancer-associated mortality (3, 4).

The clinical presentation of this condition may vary widely which is divided into following five types: Pigmented nodular type, pigmented macular type, pigmented mixed type, non-pigmented nodular type and non-pigmented mixed type (5-7).

On the other hand, cancers of a thyroid gland are the most frequent endocrine cancers, and this is known over a decades (8). Unlike other forms of thyroid cancers (medullary, follicular and anaplastic), whose occurrence remained almost the same over time, the incidence of papillary thyroid cancer strongly increased (9). Indeed, the vast majority of thyroid malignant tumors belong to papillary cancers (around 90%) (10). To date, several factors have been identified to potentiate the occurrence papillary thyroid cancer such as Hashimoto thyroiditis, other thyroid diseases, and early exposure to ionizing radiation (11, 12). Moreover, some evidence indicate that thyroid malignancy can be found more often after other primary cancers, as consequence of radiation therapy or even without it (13, 14). Therefore, much attention has been paid to the assessment of the risk for development of thyroid cancers on the field of existence of non-thyroid malignancies. Nevertheless, there are almost no literature data describing synchronous thyroid cancer and additional malignancy.

Here, we describe the case of a patient with synchronous neck melanoma and papillary thyroid cancer.

CASE REPORT

A 49-year-old man had a change on the neck at the last 3-4 months that he accidentally noticed. He had hoarse voice, was afebrile, did not sweat more than usual and feel exhausted, without rash or itching. At physical examination following was observed: on the neck - right angularly palpable one lymphatic gland (size 1,2 cm, hard painless, weakly

movable), left submental palpable one deep and more tiny single painless lymphatic gland. Supraclavicular and axillary without significant lymphatic glands, spleen palpable to 1 cm, without lymphatic glands in inguinal region, liver not enlarged, airway noise intensified in the lungs.

MR examination of the neck and upper mediastinum before the surgery indicated a hyperintense focal change in the left thyroid gland which dimensions was 19 x 15mm (AP-LL) (Figure 1A) and several hyperintense inhomogeneous lymph glands of the jugular chain, on the both sides, with different sizes (Figure 1B).

Figure 1. MR examination of the neck soft tissues. The examination was performed in the axial section and T2W FS sequences.

A) In the left lobe of the thyroid gland there is a clearly separated hyperintense focal change in size 19 x 15 mm (AP-LL). It does not penetrate the thyroid capsule.

B) In level A and 5A there are several hyperintense inhomogeneous lymph glands on both sides, with different sizes - show pathological signal intensity.

Ex tempore analysis indicated that the right lobus was benign, the left lobe was malignant, and the nodus of the right jugular chain was malignant. The pathology report showed that the nodus was most likely malignantly altered due to melanoma and advised to examine the skin of the head and neck intraoperatively. On that occasion pigmented nevus of right tragus was discovered, removed by excision, and confirmed to be malignant. On the basis of the above findings, in addition to total thyroidectomy, two-sided functional dissection of the lymph nodes of the neck was performed. After the operation, Letrox tablets was prescribed a 100 mg 1x1.

The pathohistological diagnosis of the skin with a tumor on a baseline of 15x13x12 mm, light brown color, uneven pigmentation was as follows: Melanoma nodular cutis invasivum (G-II, pT4bN1 (1 + / 4In), Breslow-3, Clark-III, L+, Vx, Ro. Ulceration of surface tumor was present, with peritumoral lymphocytic infiltration. Mitotic index was 4/10HPF, pigment production was minimal with dominant vertical growth phase. The pathohistological diagnosis of the left lobus was: Carcinoma papillary glandulae thyroideae invasivum (G-I, nG-I, pT2, Lx, Vo). The pathohistological diagnosis of the right lobus was: Struma colloides cystica diffusa glandulae thyroideae.

During the first CT of head, neck and thorax it was noticed that head and lungs imaging were normal. In the neck region at the height of the oropharynx, alongside the marginal blood vessels, there was one lymph node of 7 mm in size on both sides. Thyroid scintigraphy had shown that there was no accumulation of radioactive iodine and above the thorax finding was neat. A year later, PET/CT of the whole body was made (from the base of the skull to the proximal parts of the femur). Scanning of the entire body was done 60 minutes after i.v. injection of 9 mCi fluorodeoxyglucose with fluorine-18 (¹⁸FDG). PET/CT findings indicated that there was no rest or recurrence of the tumor.

Ultrasound of the neck was done a year after the PET/CT scan. Right in the region of the lower half of the parotid and lateral half of the submandibular gland, three changes were noticed. The largest lymph gland of clear contours was hypoechoic structure, diameter 26 x 9 mm with a clear separation of the cortical layer of the thin and slightly echogenic central matrix. Another lymph gland was with oval structure and diameter of 9 x 5 mm, and the third was in the parotid parenchyma with diameter of 12 x 4 mm. In the left region of the lateral half of the submandibular gland was the lymph gland of diameter 15 x 4mm. There were no signs of recurrence in the thyroid box region. Supraclavicular and the lateral neck chains did not had signed lymph nodes. Taking into account that right submandibular lymph nodes were 26 mm of diameter, and MR inspection was scheduled. The results of thyroid hormones and antibodies were following: PTH intact-55,4 pg/ml (15-65 pg/ml); TSH-78,629 uIU/ml (0,27-4,20 uIU/ml); TT4-0,53 nmol/l (66,0-181,0 nmol/l); TT3-0,45nmol/l (2,7-3,87 nmol/l); Anti Tg-12,5 IU/ml (< 115 IU/ml); TG-0,538 ng/ml (1.4-78 ng/ml). TSH was elevated

while TT4, TT3 and TG were lower than reference values. The dose of Letrox was increased to 150 mg daily.

MR imaging after total thyroidectomy and malignant melanoma surgery did not showed detectable recurrence of the tumor.

DISCUSSION

This case illustrates the presentation, diagnosis, and treatment of a patient with synchronous neck melanoma and papillary thyroid cancer. Literature data have shown that multiple cancers of head and neck are not infrequent malignancies and their incidence is raising (15, 16). Incidence for development of another primary cancer after discovering of the first malignancy, for synchronous cancers is 15 % (17). A careful and systematic triage is thus of the great interest for these patient. Some studies pointed out that synchronous cancers can be detected in 9-14% of patients during routine screening (17).

Malignant melanoma is an aggressive cutaneous melanocytic neoplasia. Although melanoma most commonly metastasizes to regional lymph nodes, mortality from melanoma is due primarily to distant spread to visceral organs, commonly the lungs, liver, and brain (18-20). Considering that metastasis to the thyroid gland is a very rare, after pathohistological analysis of thyroid malignanant tissue diagnosis of synchronous cancers can be confirmed, as seen it this case report.

According to their primary site, melanomas are grouped as cutaneous, ocular, mucosal, and of unknown origin; of all, mucosal melanomas are the least frequent ones (21). Head and neck mucosal melanomas (HNMMs) comprise 0.7% to 0.8% of all melanomas and less than 10% of all head and neck melanomas (22). Malignant melanoma is an aggressive cutaneous melanocytic neoplasm which often metastasizes to regional lymph nodes but whose mortality is mainly determined by tumor dissemination to visceral organs such as the lungs, liver, and brain. Although rare, HNMMs are very aggressive malignant tumors, and their prognosis is worse than that for cutaneous and ocular melanomas (23). However, the occurrence of another primary tumor such as papillary thyroid cancer complicates the diagnostic and therapeutic approach, while the clinical signs may be asymptomatic (24). The prevalence of synchronous non-thyroidal cancers in patients on surgical therapy of papillary thyroid cancer is approximately 14 % (25). The third most frequently associated synchronous non-thyroidal cancers is melanoma (26). When comparing with patients without another malignancy, those with an non-thyroidal cancers were elderly (56.4 ± 15.5 years) and had been exposed to radiation (27). Studies have shown that pathohistological features of papillary thyroid cancers are similar in patients with non-thyroidal cancer compared with ones in patients without additional malignancy (26, 27). Despite the fact that patients with an non-thyroidal cancers were detected at a more severe level of disease than those without, additional estimation of each TNM category have shown absence of statistical distinction in the

primary tumor size, or the rate of nodal or distant metastases. (27).

Having in mind that clinical signs of patients with papillary thyroid cancer are similar to those without accessorial non-thyroidal cancers, they thus must be managed equivalently. Furthermore, surgeons should rise attention of the incidence of synchronous papillary thyroid cancer with these types of cancers and take into account assessment of the neck during thyroidal cancer diagnosis.

Treatment of thyroid malignancies is primarily surgical, but the decision to operate on the patients will depend on their clinical condition, the primary site of the original tumor, presence of other metastases, the degree of dissemination, and symptoms caused by the thyroid mass (25, 26). Surgery may also be important as a palliative treatment to relieve symptoms, particularly those associated with airway compression. No consensus exists on the extent of the surgery, and most authors recommend that isthmectomy and lobectomy be performed in cases with isolated nodules, whereas total or near-total thyroidectomy should be performed in cases with multifocal disease (28).

CONCLUSION

The message from this case report is that when diagnosing and treating thyroid cancer, the observed changes in the neck lymph nodes also indicate cancers of non-thyroid pathology such as malignant melanoma.

Surgeons should rise attention of the incidence of synchronous papillary thyroid cancer with neck melanoma and take into account assessment of the neck during thyroidal cancer diagnosis. This approach will therefore strongly contribute to the prolonged survival in these patients and prevention of rapid onset of life-threatening complications.

LITERATURE

- Atkinson V. Recent advances in malignant melanoma. *Intern Med J* 2017; 47(10):1114–21.
- Longvert C, Saiag P. Melanoma update. *Rev Med Interne* 2019; 40(3): 178–83.
- Cabrera R, Recule F. Unusual clinical presentations of malignant melanoma: a review of clinical and histologic features with special emphasis on dermatoscopic findings. *Am J Clin Dermatol* 2018; 1: 15–23.
- Pavri SN, Clune J, Ariyan S, Narayan D. Malignant melanoma: beyond the basics. *Plast Reconstr Surg* 2016; 138(2): 330e–340e.
- Leonardi GC, Falzone L, Salemi R, Zanghi A, Spandidos DA, McCubrey JA, et al. Cutaneous melanoma: from pathogenesis to therapy. *Int J Oncol*. 2018; 52: 1071–80.
- Hartman RI, Lin JY. Cutaneous melanoma-a review in detection, staging, and management. *Hematol Oncol Clin North Am* 2019; 33(1): 25–38.
- Iglesias-Pena N, Paradelo S, Tejera-Vaquerizo A, Boada A, Fonseca E. Cutaneous melanoma in the elderly: review of a growing problem. *Actas Dermosifiliogr* 2019; 110: 434–47.
- Takano T. Natural history of thyroid cancer. *Endocr J* 2017; 64: 237–44.
- Luzón-Toro B, Fernández RM, Villalba-Benito L, Torroglosa A, Antiñolo G, Borrego S. Influencers on thyroid cancer onset: molecular genetic basis. *Genes (Basel)* 2019; 10: 913.
- Albi E, Cataldi S, Lazzarini A, Codini M, Beccari T, Ambesi-Impiombato FS, et al. Radiation and Thyroid Cancer. *Int J Mol Sci* 2017; 18: 911.
- Wang TS, Sosa JA. Thyroid surgery for differentiated thyroid cancer - recent advances and future directions. *Nat Rev Endocrinol* 2018; 14: 670–83.
- Ferrari SM, Fallahi P, Elia G, Ragusa F, Ruffilli I, Paparo SR, et al. Thyroid autoimmune disorders and cancer. *Semin Cancer Biol* 2020; 64: 135–46.
- Bhatti P, Veiga LH, Ronckers CM, Sigurdson AJ, Stovall M, Smith SA, et al. Risk of second primary thyroid cancer after radiotherapy for a childhood cancer in a large cohort study: an update from the childhood cancer survivor study. *Radiat Res* 2010; 174: 741–52.
- Lal G, Groff M, Howe JR, Weigel RJ, Sugg SL, Lynch CF. Risk of subsequent primary thyroid cancer after another malignancy: latency trends in a population-based study. *Ann Surg Oncol* 2012; 19: 1887–96.
- Leemans CR, Snijders PJF, Brakenhoff RH. The molecular landscape of head and neck cancer. *Nat Rev Cancer* 2018; 18: 269–82.
- Hahn LD, Kunder CA, Chen MM, Orloff LA, Desser TS. Indolent thyroid cancer: knowns and unknowns. *Cancers Head Neck* 2017; 2: 1.
- Serafini MS, Lopez-Perez L, Fico G, Licitra L, De Cecco L, Resteghini C. Transcriptomics and Epigenomics in head and neck cancer: available repositories and molecular signatures. *Cancers Head Neck* 2020; 5: 2.
- Ascierto PA, Accorona R, Botti G, Farina D, Fossati P, Gatta G, et al. Mucosal melanoma of the head and neck. *Crit Rev Oncol Hematol* 2017; 112: 136–52.
- Nenclares P, Ap Dafydd D, Bagwan I, Begg D, Kerawala C, King E, et al. Head and neck mucosal melanoma: The United Kingdom national guidelines. *Eur J Cancer* 2020; 138: 11–18.
- Green B, Elhamshary A, Gomez R, Rahimi S, Brennan PA. An update on the current management of head and neck mucosal melanoma. *J Oral Pathol Med* 2017; 46: 475–79.
- Jaballah Vinckenbosch P, Litzistorf Y, Gaide O, Özdemir BC, Michielin O, Reinhard A. ENT management of head and neck cutaneous melanoma. *Rev Med Suisse* 2020; 16: 1853–59.
- Lerner BA, Stewart LA, Horowitz DP, Carvajal RD. Mucosal melanoma: new insights and therapeutic options for a unique and aggressive disease. *Oncology* 2017; 31: e23–e32.

23. Mihajlovic M, Vlajkovic S, Jovanovic P, Stefanovic V. Primary mucosal melanomas: a comprehensive review. *Int J Clin Exp Pathol* 2012; 5: 739-53.
24. Coca-Pelaz A, Shah JP, Hernandez-Prera JC, Ghossein RA, Rodrigo JP, Hartl DM, et al. Papillary thyroid cancer-aggressive variants and impact on management: a narrative review. *Adv Ther* 2020; 37: 3112–28.
25. Haroon Al Rasheed MR, Xu B. Molecular alterations in thyroid carcinoma. *Surg Pathol Clin* 2019; 12: 921–30.
26. Costa MM, Belo S, Capela-Costa J, Costa J, Carvalho D. Malignant melanoma with synchronous thyroid metastases: case report and literature review. *Arch Endocrinol Metab* 2017; 61: 193–97.
27. Heroiu Cataloiu AD, Danciu CE, Popescu CR. Multiple cancers of the head and neck. *Maedica (Bucur)* 2013; 8 : 80–85.
28. Miccoli P, Bakkar S. Surgical management of papillary thyroid carcinoma: an overview. *Updates Surg.* 2017; 69:145–50.