Case of Synchronous Central Neck Node Metastases from Both Primary Thyroid Cancer and from Endometrial Cancer to the Thyroid

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A 54-year-old woman presenting with dizziness was diagnosed with a metastatic brain tumor. Imaging studies to identify the primary cancer revealed endometrial thickening with a left adnexal mass, enlarged bilateral external iliac lymph nodes, and multiple attenuated nodules in both lobes of the thyroid gland with enlarged central neck nodes. After curettage of the uterine endometrium and ultrasonography-guided gun biopsy of the thyroid gland to confirm uterine and thyroid cancers, respectively, total abdominal hysterectomy with bilateral salpingo-oophorectomy and total thyroidectomy with bilateral central neck dissection were performed. Histopathologic examination of the removed tissues demonstrated both endometrial carcinoma metastasis to the thyroid gland and primary thyroid cancer with synchronous central neck node metastasis originating in the endometrium and thyroid. Three of the four right central lymph nodes were positive for metastatic papillary carcinoma; on the other hand, the remaining right central lymph node and one of the two left central lymph nodes were confirmed to be positive for metastatic endometrial carcinoma. (Korean J Med 2014;86:343-348)

Keywords: Papillary thyroid cancer; Endometrial neoplasm; Lymph nodes; Lymphatic metastasis

INTRODUCTION

The head and neck region is the primary site of lymph node metastases. The most common extraoral primary site of cervical lymph node metastasis is the thyroid gland, with papillary thyroid carcinoma (PTC) accounting for up to 25-50% of cervical lymph node metastasis cases [1]. It is no wonder that 50-60% of PTC patients have central neck node metastasis [2], and 2-38% have lateral neck node metastasis at the time of initial surgery [3]. Therefore, when a patient is diagnosed with a primary thyroid
cancer, the primary differential diagnosis of enlarged central neck nodes is expected to be metastasis from the thyroid tumor.

Cervical lymph node metastasis from endometrial cancer occurs rarely, with a frequency of 0.15% [4], in the form of lateral neck node metastasis via the thoracic duct. However, once endometrial carcinoma first metastasizes to the thyroid, it may subsequently metastasize to the cervical lymph nodes.

Herein, we report a case of synchronous central neck node metastases both from primary thyroid cancer and from endometrial cancer to the thyroid.

**CASE REPORT**

A 54-year-old woman suddenly developed severe, non-whirling, constant dizziness. She was referred to our hospital after diagnosis of multiple brain tumors by brain computed tomography (CT) at a nearby hospital. Physical examination revealed abnormal blood pressure (179/101 mmHg) in the absence of additional abnormalities. She had normal neurologic functions with all results of the initial laboratory tests falling within their normal reference ranges.

Magnetic resonance imaging of the brain revealed multiple hyperintense masses with perilesional edema involving both hemispheres on a T2-weighted image, consistent with metastatic brain tumors. Further diagnostic studies were performed to investigate the primary origin of the metastatic brain tumors. Positron emission tomography (PET) revealed heterogeneously hypermetabolic masses in the pelvic cavity, mediastinum, left paraaortic lymph nodes, left femur head, and right thyroid gland. The serum TSH level was 5.97 μIU/mL (normal reference range: 0.4-4.1 μIU/mL), and the free T4 level was 1.63 ng/dL (normal reference range: 0.7-1.8 ng/dL). Additionally, there were increased levels detected of three serum tumor markers: serum levels of CA 19-9, CA 125, and CA 15-3 were 650.0 U/mL (normal reference range: 0-37 U/mL), 978.3 U/mL (normal reference range: 0-35 U/mL), and 69.2 U/mL (normal reference range: < 30 U/mL), respectively.

Chest and abdominal CT scans showed a solid and cystic endometrial mass in the left adnexa with multiple enlarged lymph nodes along the bilateral external iliac chains and bilateral mediastinum (Fig. 1A). Thyroid CT scans revealed multiple solid masses with low attenuation in both thyroid lobes (Fig. 1B), with 57 calcified lymph nodes at levels IV, V, and VI of the neck (Fig. 1C).

Ultrasonography (USG) of the thyroid demonstrated a 1.12 × 0.83 × 1.11 cm indeterminate nodule with suspicious microcalcification in the middle of the left thyroid lobe (Fig. 2A). Another indeterminate nodule (1.79 × 1.13 × 1.98 cm in size)

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**Figure 1.** Abdominal CT scans. (A) Solid and cystic endometrial mass in the left adnexa with multiple enlarged lymph nodes along bilateral external iliac chains. The left-hand arrow indicates the general endometrial mass and the right-hand arrow an enlarged lymph node. Thyroid CT scans of papillary thyroid cancer (PTC) with microcalcification and metastatic lymph nodes. (B) Masses were found in both lobes of the thyroid gland, with the left-side mass larger than the right-side mass. (C) The lymph nodes of both sides of the neck at levels IV, V, and VI were enlarged.
Figure 2. Ultrasonography (USG) imaging of the thyroid. (A) USG demonstrated an indeterminate nodule in the middle section of the left thyroid lobe. The 1.12 × 0.83 × 1.11-cm nodule was solid and ill-defined, with low echogenicity and suspicious microcalcification. (B) Another indeterminate nodule with peripheral macrocalcification (1.79 × 1.13 × 1.98 cm) was found in the left lower thyroid. (C) Multiple nodules and cysts were found in both thyroid lobes; the largest nodule was 1.66 cm long and located in the right middle thyroid. Abnormal neck lymph nodes were not found, because we did not use USG to examine the neck region.

Figure 3. Endometrial adenocarcinoma. (A) Endometrial adenocarcinoma showing a cribriform pattern in the uterine endometrium. (B) Metastatic endometrial adenocarcinoma in the ovary. (C) A poorly differentiated portion of metastatic endometrial adenocarcinoma in the ovary. (D) Poorly differentiated metastatic adenocarcinoma within the thyroid gland. Its morphology was identical to that of the poorly differentiated portion of the endometrial adenocarcinoma in the ovary. (E) A poorly differentiated metastatic adenocarcinoma in the parafollicular area of the neck lymph node (All pictures were taken at × 200 magnification).

with peripheral macrocalcification was observed in the left lower thyroid (Fig. 2B). Following surgical removal, these two nodules were confirmed to be PTC. Multiple other nodules and cysts were found in both thyroid lobes and, among them, the largest nodule was a 1.6-cm well circumscribed mixed nodule located in the right middle thyroid (Fig. 2C), unexpectedly confirmed as metastatic endometrioid carcinoma following surgery. Bone scans revealed hot uptake on the left femoral
head, which was consistent with bone metastasis.

Curettage of the uterine endometrium and USG-guided gun biopsy of thyroid nodules were performed to confirm grade 2 endometrial carcinoma and PTC, respectively.

Based on the above observations, the patient was diagnosed with synchronous double primary malignancies: primary endometrial cancer with metastasis to the ovaries, paraaortic nodes, brain, and bone (left femur head), together with primary thyroid cancer with suspicious central neck node metastasis.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy and total thyroidectomy with bilateral central neck dissection were performed simultaneously. For the brain lesion, 15-22 Gy gamma-knife surgery was conducted.

Pathologic examination revealed adenocarcinoma with a cribriform glandular pattern, consistent with endometrial carcinoma (Fig. 3A), with myometrial invasion extending to the cervix and bilateral ovaries and mesosalpinges (Fig. 3B and 3C). The thyroid specimen showed nodules of various sizes and diverse natures: 1) left and right thyroid tumors presented as solitary, non-encapsulated solid tumors with ill-defined capsular invasion, measuring up to 1.0 × 0.5 cm, with a papillary structure covered by a single layer of cuboidal epithelial cells containing grooved and clear nuclei, consistent with the classical type of papillary carcinoma (Fig. 4A and 4B); 2) a 0.8 × 0.7 × 0.6 cm calcified nodule containing gelatinous materials in the right lobe was consistent with the follicular variant of papillary carcinoma and showed irregularly shaped follicles with cuboidal epithelial cells containing grooved and clear nuclei (Fig. 4D and 4E); and 3) a 1.4 × 1.2 × 0.9 cm nodule containing gelatinous materials was identified as adenocarcinoma with a cribriform glandular pattern with extensive angiolymphatic tumor emboli, identical to the poorly differentiated endometrial adenocarcinoma found in the ovaries (Fig. 3D). Interestingly, three of the four resected right central nodes were confirmed to be positive for metastatic papillary carcinoma (Fig. 4C); on the other hand, the remaining right node and one of two resected left nodes were
positive for metastatic endometrial adenocarcinoma (Fig. 3E). The other left node showed reactive changes.

Despite the aggressive treatment, the patient developed new metastases in the brain, liver, and adrenal glands. She died 21 days after surgery.

**DISCUSSION**

While many subtypes of PTC have been reported, classical PTC, found in 80% of cases, is the most common variant. Metastasis to cervical lymph nodes is reported in 50-60% of patients with classical PTC (up to 90% for occult metastases) [2]. In the follicular variant of PTC, neck node metastasis does not commonly develop [5]. Moreover, cervical lymph node metastases from endometrial carcinoma are extremely rare; only 0.15% of cases of neck node metastasis from gynecological malignancies have been confirmed as endometrial carcinoma [4]. Additionally, the metastatic neck nodes in endometrial carcinoma are most often located in the left supraventricular node, or at level III or IV. Only a single case report exists on cervical lymph node metastasis of endometrial carcinoma, describing metastasis to the left anterior neck [6].

Metastasis to the central lymph nodes from endometrial cancer, as shown in our patient, has not been reported previously, and this metastasis rarely derives from primary endometrial cancer directly. The central nodes (level VI) are commonly regional nodes of the thyroid, and endometrial cancer more frequently forms metastatic lesions in neck nodes other than the central nodes, as mentioned above. Therefore, the metastases in the cervical nodes from endometrial cancer are suspected to be from metastasis of endometrial carcinoma to the thyroid gland, which is also very rare, rather than from primary endometrial cancer.

The carcinoma that most commonly metastasizes to the thyroid is renal cell carcinoma (> 50% rate), followed by lung cancer and gastrointestinal malignancies, then mammary gland cancer and malignant melanoma [7]. Only a few reports have described metastasis of endometrial cancer to the thyroid [8].

In our patient, as well as the rare metastasis to the thyroid itself, the bilateral central neck metastasis from endometrial cancer may also suggest a form of endometrial cancer more aggressive than the coexisting primary PTC, which was limited to the ipsilateral nodes.

There is no distinguishing characteristic of metastatic lesions in the head and neck areas that indicates the origin of the primary cancer. Calcification and cystic changes were reported in 26-54% and 6% of node metastases from primary thyroid cancers, respectively [9], but never for metastasized tumors originating from endometrial cancer. In the present case, the calcified thyroid nodule and central nodes were proven to be PTC, while the cystic thyroid nodule was confirmed as metastatic endometrial carcinoma. Using imaging methods, we could not determine whether the thyroid nodules and/or accompanying lymphadenopathies were primary or metastatic cancer. Therefore, the clinical diagnosis of coexisting cancers must be taken into consideration when verifying the origin of cervical node metastases.

Unfortunately, our patient died only 3 weeks after the treatment she received, which raises questions about the necessity of the treatment. Surgery is the treatment of choice for endometrial cancer, and surgical staging is recommended by the International Federation of Gynecology and Obstetrics (FIGO), because pelvic exenteration and cytoreductive surgery may improve survival even in cases of advanced or recurrent endometrial cancer [10]. Our patient was approved for surgery followed by postoperative chemotherapy for endometrial cancer, because it was difficult to predict such a poor prognosis, since the patient and her family were eager to pursue active treatment and since the patient had a good performance status. Simultaneous surgery to remove the thyroid cancer was also planned based on the possibility that surgical removal might be a sufficient treatment with relatively low predicted morbidity.

In summary, the patient in this case was diagnosed with synchronous double primary malignancies: 1) primary endometrial cancer with metastasis to the thyroid gland and bilateral central neck nodes, as well as to the ovaries, paraaortic nodes, brain, and bone (left femur head), and 2) primary thyroid cancer with central neck node metastasis. Central neck lymph node
metastasis originated from two entirely different cancers.

중심 단어: 갑상선암; 자궁내막암; 림프절전이

REFERENCES