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Case Report

A synchronous medullary and papillary thyroid carcinoma

Oscar Varela-Cano[1], Zelik Luna-Peteuil[2], Kuauhyama Luna-Ortiz[1]*

[1]Department of Head and Neck Surgery at Instituto Nacional de Cancerología, Ciudad de México, Mexico
[2]Universitatea de Medicinâ și Farmacie Grigore T. Popa, Iași, Rumania

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***Correspondence:**
Dr. Kuauhyama Luna-Ortiz,
E-mail: kuauhyama@yahoo.com.mx

ABSTRACT

The synchronous occurrence of medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC) is rare (<1%). The medullary component determines the prognosis. A 31-year-old female with no relevant personal or family cancer history presented with swelling on the right side of the neck. A fine-needle aspiration biopsy was positive for MTC and PTC. Mass sequencing of 322 genes associated with cancer came back negative. The histopathological examination revealed synchronous MTC and PTC with thymic and bilateral lymph node metastasis. The patient underwent total thyroidectomy with bilateral radical neck dissection (II-V), central dissection, and mediastinal dissection including the thymus. The extent of surgery is determined by MTC and the analysis of RET and BRAF mutations. Post-operative treatment must include monitoring for specific markers (calcitonin and thyroglobulin, respectively, for MTC and PTC). Based on histopathological results and recurrent PTC, TSH suppression and iodine-131 therapy should be considered. Recurrent MTC must be treated with new targeted therapies.

Keywords: Synchronic papillary and medullary tumor, Cancer, Treatment

INTRODUCTION

Thyroid cancer is one of the most common neoplasms worldwide. Papillary carcinoma, originating from follicular cells, accounts for 90% of cases. Medullary carcinoma, originating from C-cells that secrete calcitonin, is less common; its incidence has remained unchanged at about 5%.[1,2] The prognosis varies depending on the type of carcinoma; unlike medullary carcinoma, papillary carcinoma has high survival rates (>90%). The synchronous occurrence of two or more types of thyroid cancer is extremely rare (<1% of all cases).[3] Synchronous tumors refer to cases where two or more tumors are diagnosed within 6 months of the primary tumor, most of them are of metastatic origin. Roughly 92 cases had been reported worldwide until 2011, and 7 more cases have been reported since then.[3-8] The purpose of the present paper is to highlight the management of such rare cases; however, medullary carcinoma carries a worse prognosis.

CASE REPORT

A 31-year-old female was referred to our hospital with a history of four months of swelling of the anterior part of the neck, affecting the left thyroid lobe. After undergoing an ultrasound-guided fine-needle aspiration biopsy, she was diagnosed with MTC. The right thyroid lobe measured 1.5×1.3 cm, and the left lobe was 3.7×2 cm.

We confirmed the diagnosis and performed genetic testing to identify mutations. The ultrasound findings were also confirmed. Bilateral adenopathies measuring 37×20×21 were observed; those on the left side did not show signs of malignancy, but several right-sided nodules were suspicious for malignancy (TI-RADS 5) in levels III, IV, and VB. Calcitonin and calcium levels were 11166 pg/ml and 7.7, respectively. Mass sequencing of 322 genes associated with cancer came back negative. The patient underwent total thyroidectomy with bilateral radical neck dissection (II-V), central dissection, and mediastinal dissection including the thymus (Figure 1).

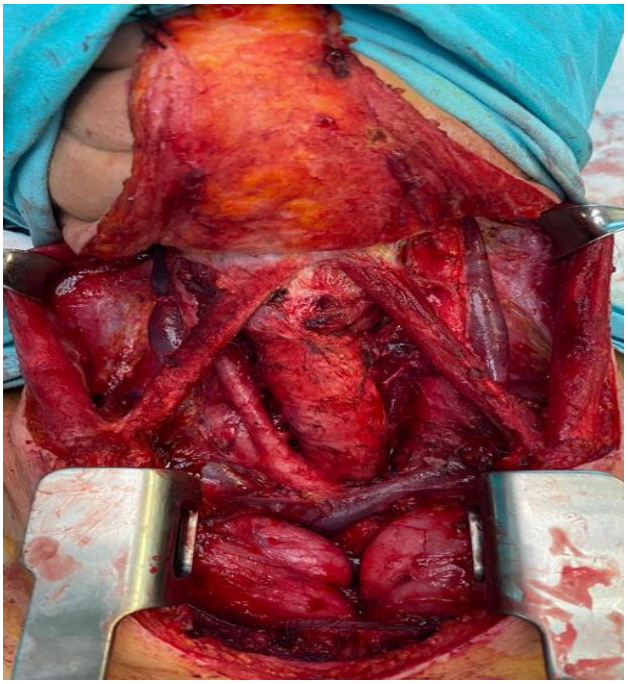

Figure 1: Patient under treatment for MTC at our hospital, where total thyroidectomy with bilateral radical neck dissection (II-V), central dissection (VI), and mediastinal dissection (VII) including the thymus are performed. Neuromonitoring and locating of parathyroid glands, especially the superior ones.

The histopathological results indicated the following: Left MTC, measuring 2.2×3.7 cm, lymphatic permeation, and extracapsular extension with infrahyoid muscles infiltration. The right radical neck dissection yielded 7 positive nodes out of 34, while the left radical neck dissection yielded a nodal mass and 39 positive nodes out of 54. Finally, the central dissection yielded 4 positive nodes out of 5; the thymus showed infiltrating foci of 3 mm. Stage IVA T3bN1bM0.

Right PTC, measuring 7 mm, multifocal, non-encapsulated; right thyroid lobe and isthmus, lymphovascular permeation. The right radical neck dissection yielded 3 positive nodes out of 33, the left radical neck dissection yielded 54 negative nodes, and the central dissection yielded 1 positive node out of 5; the thymus showed infiltrating foci of 9 mm. Stage IVA T1N1bM0.

The patient refused iodine-131 therapy. During her evolution she exhibited elevated calcitonin levels, so she underwent ^{68}Ga-DOTATOC PET/CT, which showed neoplastic activity in the lungs. Then she was examined with ^{18}FDG and ^{18}F-DOPA PET/CT, which revealed more neoplastic sites in the liver and elevated calcitonin. The lung findings agree with PTC, which is associated with increased serum thyroglobulin 2 years after surgery and normal parathormone levels. The patient decided to try alternative medicine even though she was being treated in our hospital.

DISCUSSION

The synchronous occurrence of two or more types of thyroid cancer is extremely rare (<1% of all cases of thyroid cancer).[3] Roughly 92 cases had been reported worldwide until 2011 and 7 more cases have been reported since then.[3-8] The criteria to diagnose synchronous malignant tumors have already been defined: 1) tumors must be clearly malignant as determined by histological analysis; 2) each tumor must be topographically separate and distinct; 3) the probability that one is a metastatic lesion from the other must be ruled out.[9,10]

Even though the diagnostic approach of thyroid tumors is indistinct and independent of the histopathological diagnosis, it allows us to provide initial treatment based on histological findings, as in the present case where the initial diagnosis of MTC was made using fine-needle biopsy. In our hospital MTC is initially treated with total thyroidectomy with bilateral radical neck dissection (II-V), central dissection, and mediastinal dissection including the thymus (Figure 1).[11] However, if PTC had been diagnosed first, the treatment would have been suboptimal from our point of view. Wong et al described finding a secondary tumor incidentally after a thyroidectomy.[12] An easy option to avoid this would be to ask all patients to include calcitonin levels in their preoperative thyroid function tests. The final histopathological report of the present case showed similar infiltration in both tumors with positive neck and mediastinal nodes.

Adjuvant treatments vary; for MTC if there are elevated calcitonin levels, patients would be candidates for new targeted therapies because MTC has the worst prognosis. PTC has a poor prognosis; it is thus important to treat it in the usual way, with iodine-131 therapy. Our patient did not accept any other therapy.

Follow-up should be appropriate for each disease. MTC patients should only receive hormone replacement therapy, but we had to change the treatment to hormone suppression due to the papillary component of our patient.

It is important to perform genetic tests to differentiate a sporadic from a familial MTC. If the latter is demonstrated, the parents, siblings, or children of the patient should also undergo genetic testing. In the present case the mass sequencing of 322 genes, including RET and BRAF, was negative. According to Fibbi et al 92 cases of synchronous PTC and MTC were published from 1981 to 2012.[3] In 53 of such cases, it was not possible to determine whether it was a sporadic or familial cancer because genetic testing was not performed, 10 were familial cancer (6 MTC and 4 PTC), and 29 were sporadic. We found 6 cases in our review from 2011 to 2020, all of which were described as sporadic due to negative RET and BRAF mutations.

CONCLUSION

The occurrence of synchronous double primary MTC and PTC is extremely rare. We should be careful when establishing the primary one to avoid suboptimal treatment. Preoperative calcitonin levels are always helpful. Post-operative management and long-term follow-up should be in line with the double primary cancer. The patient's relatives should undergo genetic testing.

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