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CASE REPORT
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Marine–Lenhart Syndrome with Unilateral Orbitopathy and Metastatic Thyroid Papillary Carcinoma to Lymph Node

ABSTRACT

Marine–Lenhart syndrome is a name given to the coexistence of Graves' disease and functional nodules. In this rare syndrome, nodules are mostly benign. The most common extrathyroidal manifestation of Graves' disease is Graves' orbitopathy. It is usually seen bilaterally but can also be seen unilaterally. In this article, a case with Marine–Lenhart syndrome, metastatic thyroid papillary carcinoma, and unilateral Graves' orbitopathy is presented.

Keywords: Marine–Lenhart syndrome, orbitopathy, thyroid papillary carcinoma

Introduction

Marine–Lenhart syndrome is the name given to the coexistence of thyroid hyperfunctioning nodules and Graves' disease.[1] Thyroid scintigraphy typically shows both increased uptake in the affected nodule(s) and increased activity in the extranodular thyroid tissue. Usually, thyroid hyperfunctioning nodules are benign, and malignancy in hyperfunctioning thyroid nodule is rare. The frequency of follicular thyroid carcinoma has increased compared to the general population.[2] The risk of malignancy in patients with hyperfunctioning nodules and Graves' disease is commonly underestimated. Graves' orbitopathy is relatively rare. The estimated incidence of all cases of Graves' orbitopathy is 0.54 to 3.3 cases per 100 000, with mild and nonprogressive cases being more common.[3] Graves' orbitopathy is generally bilateral, but rarely unilateral forms can be observed.[4]

Here, we present a rare case of Marine–Lenhart syndrome, metastatic thyroid papillary carcinoma, and unilateral Graves' orbitopathy. In previous studies, several cases have been reported but Marine–Lenhart with unilateral orbitopathy and thyroid papillary carcinoma is uncommon. Informed consent to publish the picture and information were obtained from the patient.

Case Presentation

A 30-year-old man was referred to our endocrinology outpatient clinic by his ophthalmologist because of abnormality in thyroid tests. His main complaint was redness of the right eye for the past 2 weeks. He was symptomatic for occasional palpitations. He had no history of thyroid disease, radiation to the head and neck region, systemic disease, alcohol, and medications use. In his family history, his father had thyroid papillary carcinoma. On physical examination, his blood pressure was 120-70 mm Hg and pulse rate was 115 beats/min. Thyroid gland was not palpated. Eye examination was characterized by unilateral right exophthalmos, conjunctival erythema, and eyelid redness (Figure 1). Bilateral visual acuity was normal. The Clinical Activity Scale (CAS) was 2/7 points due to the eyelid redness and conjunctival injection. Hertel exophthalmometer measurement was 23 mm on the right and 17 mm on the left. Systemic examination was unremarkable. Laboratory tests showed a suppressed thyroid stimulating hormone (TSH) level of 0.02 mU/L (normal 0.35-4.94 mU/L) and elevated levels of free thyroxine (fT4) 1.6 ng/dL (normal 0.7-1.48 ng/dL) and free triiodothyronine (fT3) 6.1 ng/dL (normal 2-4.4 ng/dL). Thyroid autoantibody tests (thyroid peroxidase antibody and thyroglobulin antibody) were positive. Thyroid stimulating hormone receptor stimulating antibody (TSIab) level was elevated (4 IU/L; reference <0.10). Laboratory evaluation revealed normal complete blood counts and serum electrolytes, blood glucose,

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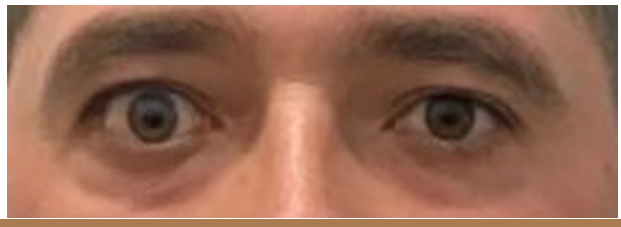

Figure 1. Eye examination reveals unilateral right exophthalmos, conjunctival erythema, and eyelid redness.

creatinine, and liver functions. In thyroid ultrasonography, both thyroid lobes were in normal size and thyroid parenchyma was heterogeneous. Thyroid vascularity was increased. Thyroid ultrasonography demonstrated a heterogeneous, hypoechoic, irregularly demarcated nodule, measuring 14 × 10 mm with punctate calcification within the superior pole of the right thyroid lobe and lymphadenopathy, which is measuring 21 × 12 mm, hypoechoic, with microcalcifications and without a hilus in the right cervical level 3. Thyroid scintigraphy with technetium-99m revealed a diffusely homogenous uptake throughout the gland and a focal uptake in the right upper lobe corresponding to the hypoechoic nodule detected in ultrasonography (Figure 2). Orbital magnetic resonance imaging (MRI) showed unilateral right-sided exophthalmos predominantly caused by the thickening of the retro-orbital tissue.

Thyroid fine-needle aspiration biopsy (FNAB) was performed due to malignant ultrasonography features of the nodule and thyroglobulin washout, and biopsy was performed from right cervical level 3 lymphadenopathy. The FNAB of the nodule was benign, but FNAB of the lymphadenopathy was malign and thyroglobulin (tg) washout measurement of right cervical level 3 lymphadenopathy was positive (tg: 5000 µg/L). The patient became euthyroid after 6 weeks with methimazole 5 mg/day treatment. The patient underwent total thyroidectomy and right central and right lateral lymph node dissection. Pathology result is unifocal, right lobe localized, 5 × 5 mm in size, classical variant, with clean surgical margins, with lymphatic invasion, thyroid papillary microcarcinoma without vascular invasion, and at right level 3, it was in the form of 1 lymph node metastasis with a diameter of 15 mm, without capsule and non-capsule spread. While the tumor diameter is 14 × 10 mm in ultrasonography, the tumor diameter is 5 × 5 mm in the pathology result because the tumor is a part of the same nodule. Postoperative thyroglobulin level was negative, and no residue was detected in the control neck ultrasonography. Levothyroxine treatment was initiated, and radioactive iodine (RAI) therapy was given.

Discussion

The occurrence of Graves' disease and autonomously functional thyroid nodules is known as Marine–Lenhart syndrome, but the diagnostic criteria for this syndrome is not well defined. D. Marine and C. H. Lenhart first described this syndrome in 1911.[5] The name Marine–Lenhart syndrome was coined by David Charkes in 1972. He described 10 patients with Graves' disease and functional nodules, defined by the following features[1]: (a) increased radioiodine uptake with one or more functional nodules in the thyroid gland in a patient with hyperthyroidism; (b) failure of TSH to alter the scintigraphic appearance of the thyroid gland; (c) stimulation of overall radioiodine uptake by TSH; (d) stimulation of radioiodine uptake by the nodule by TSH, 1.7-fold or greater. Marine–Lenhart syndrome is reported to be quite rare with a prevalence of 0.8%-4.3% in patients with Graves' disease.[1,6,7]

MAIN POINTS

- Marine–Lenhart syndrome is known as the coexistence of thyroid hyperfunctioning nodules and Graves' disease.
- Hyperfunctional thyroid nodules are usually benign, but malignancy is rare.
- The coexistence of Marine–Lenhart syndrome, unilateral orbitopathy, and metastatic thyroid papillary carcinoma is a rare entity.

Figure 2. Thyroid scintigraphy shows widespread homogeneous involvement in the entire gland and focal involvement in the right upper lobe.

Thyroid nodules can be detected in 25%-30% of patients with Graves' disease.[8-10] Although these nodules are mostly cold, benign, and multiple, only a few (1%-2.5%) are autonomous hot nodules.[1,11] The incidence of thyroid cancer in Graves' patients varies greatly. A recent meta-analysis found the incidence of thyroid cancer in Graves' patients 2.5 times higher than in the general population.[12] In previous studies, the incidence of thyroid carcinoma in Graves' patients has been reported to vary between 2% and 33.7%.[9,13-17] The incidence of thyroid cancer was found to be higher, especially in Graves' patients treated surgically.[17,18] It was thought that the high incidence of thyroid cancer in Graves' patients may be related to the ultrasonography routinely performed during the follow-up of the disease.[19] In addition, in some studies, it has been determined that thyroid cancers seen in Graves' patients have a worse clinical course than thyroid cancers seen in euthyroid patients.[20,21] In the literature, Marine-Lenhart syndrome reported with hot or cool nodules are described with Graves' disease.[22,23] Cases of thyroid papillary carcinoma accompanying Marine-Lenhart syndrome have been reported.[24,25] In our case, because the nodule had malignant characteristics and at the same time a pathological lymph node was detected in the right cervical 3, FNAB was performed from both the thyroid nodule and the pathological lymph node in the right cervical level 3, and thyroid papillary microcarcinoma was diagnosed.

The oftenest extrathyroidal presentation of Graves' disease is orbitopathy. Graves' orbitopathy is an autoimmune disease of the retro-orbital tissues.[26] Graves' orbitopathy is relatively rare (estimated

incidence: 0.54-0.9 cases/100 000/year in men, 2.67-3.3 cases/100 000/year in women), with the majority of cases being mild and nonprogressive. Moderate–severe forms account for 5%-6% of all cases.[27,28] The diseases often occur bilaterally. Unilateral orbitopathy can be seen in 9%-15% of Graves' patients.[3,4,29] In our case, unilateral Graves' orbitopathy was detected both clinically and radiologically. In our case, CAS was determined as 2/7 points.

The preferred methods in the treatment of Marine-Lenhart syndrome are RAI therapy or surgery. Surgery should be preferred if there is concomitant malignancy, moderate–severe orbitopathy, large or symptomatic compressive goiter, and patient preference. In our case, although the nodule FNAB was benign, surgical treatment (total thyroidectomy and right central and right lateral lymph node dissection) was preferred because the FNAB of lymphadenopathy at right cervical level 3 was malignant and thyroglobulin (tg) washout was positive.

Conclusion

The coexistence of Marine-Lenhart syndrome, unilateral orbitopathy, and thyroid papillary carcinoma is a rare entity. To our knowledge, only one case reported Marine-Lenhart syndrome associated with unilateral orbitopathy and metastatic thyroid papillary carcinoma. Although malignant potential of hyperfunctioning thyroid nodules is low, clinicians should keep in mind that malignancy may also be seen in hyperfunctioning thyroid nodules. Careful evaluation should be made and appropriate treatment should be applied.

Informed Consent: Informed consent to publish the picture and information were obtained from the patient.

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Declaration of Interests: The authors declare that they have no competing interest.

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