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Case Report

Internal Medicine Section

Marine-Lenhart Syndrome- A Curious Case of Thyrotoxicosis

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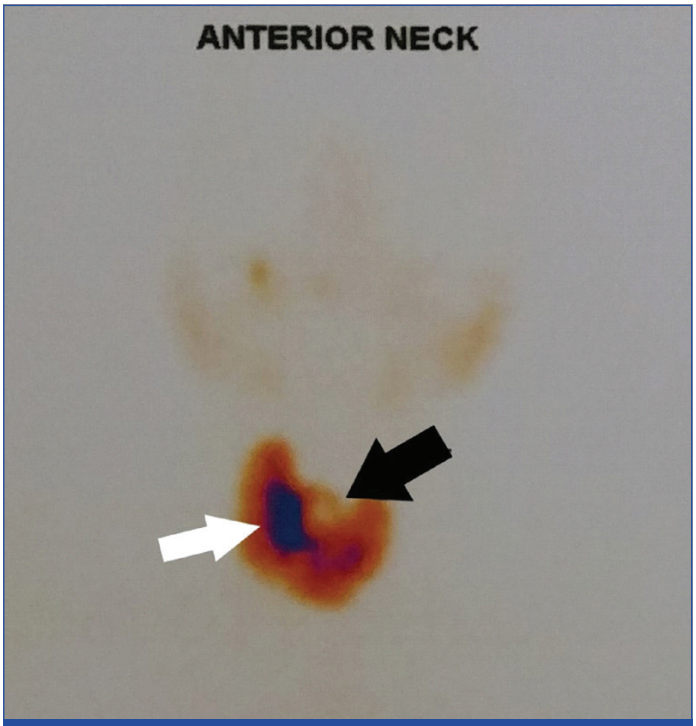
ABSTRACT

Hyperthyroidism is one of the common prevalent endocrine problems. The common causes of hyperthyroidism include Graves' disease, toxic nodular goiter and toxic adenoma. The diagnosis is usually straightforward but can be challenging at times. Marine-Lenhart syndrome refers to the rare co-existence of hyperfunctioning nodule in presence of Graves' disease. The disease can easily be misdiagnosed if clinical vigil is not high. The disease differs from classical Graves' disease in terms of clinical course, management modality and outcome. Here we present a case of 52 years old female with complaints of weight loss, excessive sweating, tremors and palpitation for last six months and swelling in antrior aspect of neck for last four months. Technetium 99 m thyroid scintigraphy showed presence of diffuse increased tracer uptake 15% with suppression of background activity. Based on these findings, a diagnosis of Marine-Lenhart syndrome was made. Early and corrected identification of this rare variant is essential for proper therapeutic management.

Keywords: Goitre, Graves' disease, Thyroid, Thyroid nodule

CASE REPORT

A 52-year-old female presented with symptoms of weight loss, excessive sweating, tremors and palpitation for last six months. She had also noticed swelling in anterior aspect of neck for last four months. She did not have any prior history of thyroid related illness, neck surgery or irradiation. There was no history of thyroid disorders among family members. She was lean (body mass index -19.4 kg/m^2). There was presence of tachycardia (heart rate- 110/min). A grade 2 firm and non tender goiter was palpable. Furthermore, a nodule of approximate size 1×2 cm was palpable over isthmus and adjacent right lobe of thyroid. There was no appreciable bruit heard over the gland. There was no associated cervical lymphadenopathy. There was no evidence of dysphagia or dysphonia. No obvious ophthalmopathy or dermopathy were present. Significant positive findings from systemic examination included presence of fine tremors and increased deep tendon reflexes. Based on frank features of thyrotoxicosis, a thyroid function test was done. The results revealed elevated free triiodothyronine (9.8 pmol/L, normal: 3.1-6.8 pmol/L), elevated free thyroxine (39.2pmol/L, normal: 12-22 pmol/L) and suppressed Thyroid Stimulating Hormone (TSH) level (0.048 mIU/mL, normal: 0.4-4.2 mIU/mL). Anti TSH receptor antibody titres were positive 14.4 IU/L (positive >2 IU/L). Complete blood count, liver function tests and renal function tests were within normal limit. Ultrasonography of thyroid showed presence of diffuse thyroid enlargement with heterogeneous parenchyma and increased parenchymal vascularity. Multiple tiny hyoechoic nodules were also noted in thyroid parenchyma. A hypoechoic nodule of size 1.5×2 cm with increased intranodular vascularity (without any microcalcification) was also noted which corresponded to the clinically palpable dominant nodule. Fine needle aspiration cytology from the same nodule did not revealed any features of malignancy. Technetium 99 m thyroid scintigraphy showed presence of diffuse increased tracer uptake 15% (normal: 0.4-1.5%) with suppression of background activity [Table/Fig-1]. A hyperfunctioning nodule with a cold area located superiorly was also noted in isthmus corresponding to clinically palpable nodule [Table/Fig-1]. Based on above findings, a diagnosis of Marine-Lenhart syndrome was made. The patient was started on anti-thyroid drugs namely (carbimazole 30 mg/day) and beta blockers for symptomatic relief. She was rendered euthyroid after three months of anti-thyroid drug treatment. She was counselled regarding role of definitive therapy (radioiodine therapy or total thyroidectomy) for management of her condition. She chose to undergo total thyroidectomy and hence was referred for the same.



[Table/Fig-1]: Technetium 99m thyroid scan showing diffuse increased tracer uptake in thyroid gland suggestive of hyperfunctioning. Also noted are a hyperfunctioning nodule in region of isthmus (white arrow) and cold area located superiorly (black arrow) suggestive of Marine-Lenhart syndrome.

DISCUSSION

Graves' disease and toxic nodular goitre are among the common causes of thyrotoxicosis seen in clinical practice. The two clinical conditions however differ in their clinical course and management strategies. It is well known that Graves' disease is an autoimmune thyroid disease which is caused due to stimulation of thyroid gland by endogenous production of stimulating TSH receptor antibodies.

However, the genesis of autonomously functioning thyroid nodule (Plummer's disease) is believed due to clonal proliferation of thyroid cells independent of TSH. Hence, the two diseases have distinct aetiopathogenesis. Marine-Lenhart syndrome refers to the rare clinical condition in which Graves' disease and autonomous functioning nodule coexist [1]. The disease may pose as diagnostic and therapeutic difficulty during evaluation. Its early recognition and differentiation from classical Graves' disease is essential for treating the condition more effectively.

The first description of the disease dates back to 1911, when the coexistence of Graves' disease and autonomously functioning thyroid nodule was described for the first time by Marine and Lenhart [2]. In 1972, Charkes ND coined the term Marine-Lenhart syndrome in honor of physicians who were first to describe this entity [1]. In his paper, Charkes ND described 10 patients with Graves' disease and functioning nodules and also proposed a set of criteria for diagnosis of this disorder. The reported prevalence of such association ranges from 2.7% to 4.1% [1].

Apart from diffuse enlargement of thyroid gland, there is increased prevalence of nodules in thyroid parenchyma in Graves' disease. The reported prevalence of thyroid nodules in cases of Graves' disease is around 25-30% [3,4]. The majority of such nodules are hypoactive (more than 95%) and a small fraction remains hyperactive. Hence from a clinical point of view, hyperfunctioning nodules in Graves' disease contribute and accentuate the degree of thyrotoxicosis. Therefore, thyrotoxicosis in Marine–Lenhart syndrome could be attributed to Graves' disease in addition to the hyperfunctioning nodule. These nodules could be hyperfunctioning from the beginning or may become so after a variable time period [5-7]. The following criteria have been proposed for diagnosis of Marine-Lenhart syndrome. These include; a) the thyroid scan shows an enlarged gland and one or more poorly functioning nodules; (b) the nodule is TSH-dependent and the peri-nodular tissue is TSH-independent; (c) after endogenous or exogenous TSH stimulation, the return of function can be demonstrated in the nodule; and (d) the nodule is histologically benign [1,8].

Review of the published cases [6-16] of Marine-Lenhart syndrome in literature reveal that nuclear imaging pattern of thyroid gland showed diffuse increased tracer uptake in thyroid gland along with further increased tracer uptake by nodules [6,9]. Initial scintigraphy pattern described in majority of cases include hyperactivity in the thyroid parenchyma with relative hypoactivity ("cold appearing") in the nodule [6,10-13]. However, cases of Marine-Lenhart syndrome showing increased tracer uptake ("hot appearing") in these nodules have also been clearly described [6,9,14-16]. Therefore, both cold and hot appearance of these hyperfunctioning nodules has been described in thyroid scintigraphy.

The lack of uptake of tracer in the nodule is attributed to suppression of thyroid tissue within the nodule by over activity of the remaining gland and hence does not take up tracer or radioactive iodine [6]. Therefore, nuclear imaging scan play a pivotal role in identification of this particular subtype of disease. Early identification is also essential for planning appropriate management strategies. Apart from diagnostic dilemma, Marine-Lenhart syndrome also poses a therapeutic challenge to treating physician because this variant is more resistant to radioiodine therapy than conventional Graves' disease [1,16]. The amount of radioiodine required for treating hyperthyroidism in such patients is higher than doses employed to treat diffuse toxic goiter [16]. An interesting facet is the development of Graves' disease shortly after radioiodine therapy for autonomously functioning thyroid nodules [17,18].

Another important clinical issue which needs mention is the presence of thyroid malignancy in the nodules reported among patients with Graves' disease. It has been reported that around 1.1% to 7.1% of patients with Graves' disease may have concomitant thyroid cancer [19,20]. Majority of thyroid carcinoma arise from cold nodules in such individuals. The most commonly reported variety is the papillary thyroid carcinoma [21]. The presence of papillary thyroid carcinoma has also been reported very rarely in patients with Marine-Lenhart syndrome [13,21]. Some authors have suggested increased aggressiveness of thyroid malignancy associated with Graves' disease [22,23] but these findings were not replicated by few other authors [24,25].

CONCLUSION(S)

To conclude, this case report exemplifies the rare occurrence of Marine-Lenhart syndrome as an underlying cause of thyrotoxicosis. Nuclear imaging scan play a pivotal role in recognition of this rare nodular variant of Graves' disease. It should be remembered that this disease is particularly resistant to radioiodine therapy in contrast to classical Graves' disease. Hence, knowledge about this rare variant among physicians is essential for early identification and appropriate intervention.

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