Marine-Lenhart-Syndrome

Poster No.: C-1801
Congress: ECR 2010
Type: Educational Exhibit
Topic: Head and Neck
Authors: J. Fernandez Sanchez; Stuttgart/DE
Keywords: Marine-Lenhart Syndrome, Scintigraphy, Color Doppler Ultrasound
DOI: 10.1594/ecr2010/C-1801

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method is strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

- What is Marine-Lenhart Syndrome ?.
- Pathology
- Diagnosis: laboratory and imaging findings.
- Treatment.

Background

Introduction

The association of Graves disease (also known as "diffuse toxic goiter" such as Basedow disease or Morbus Basedow in German speaking countries) with autonomously functioning thyroid nodules constitutes the Marine-Lenhart Syndrom (MLS).

Robert Graves first identified the association of goiter, palpitations, and exophthalmos in three cases in 1834, although Caleb Parry had published details of a case in 1825. Carl von Basedow described exophthalmic goiter in a relatively large number of cases in 1844. It was Henry Plummer in 1911 who clearly distinguished exophthalmic goiter from adenomatous goiter. But at the same year, 1911, David Marine and Carl Lenhart described hyperhyroidism due to Graves disease and concomitant functioning follicular thyroid adenomas in 8 cases. Consequently, this syndrom has been named in their honour.

Incidence
Graves disease has an annual incidence of about 5 per 10,000 people and it is the most common cause of hyperthyroidism (70-80%) followed by autonomously functioning thyroid nodules. In USA the incidence of extrapolations for Graves´ diseases is about 136,000 cases per year, the prevalence of MLS appears to lie between 2.7 and 4.1%. In selected patients with hyperthyroidism remitted to our hospital for radiodine therapy in the last 8 years the incidence of MLS was 3%.

Pathology

Graves´ disease is an autoimmune disorder, meaning the immune system makes antibodies called thyroid-stimulating immunoglobulin (TSI), which bind to and activate the thyrotropin receptor on thyroid cells attaching them. TSI mimics the action of TSH and stimulates the gland to increase thyroid hormones T3 and T4.

Solitary toxic nodule or toxic multinodular (Plummer´s disease) are usually hyperfunctioning follicular adenomas releasing thyroid hormones.

Therefore, Graves´ disease and toxic nodular goiter both causes thyreotoxicosis by different pathophysiological mechanisms, but in the MLS there is a coexistence of both pathologies.

The pathogenesis of MLS is not clear and may be as follows:

1. Initially hyperthyreodism caused by Graves disease followed later with toxic nodules
2. Initially development of autonomously functioning thyroid nodules followed later by Graves disease
3. Both pathologies are instaured simultaneously

Genetics alterations of the TSH receptors and the presence of TSH antireceptors autoantibodies in the development of MLS have been postulated.

In some case reports a hyperthyroidism induced only by a toxic nodule with additional orbitopathy considered as only manifestation of euthyroid Graves disease has been hypothesized.

Besides, radiodine therapie with I 131 could be an activating factor

Clinical presentation

The most common signs/symptoms of MLS are the same for every cause of hyperthyroidism: nervosity, palpitations, loss of weight despite increased apetite, increased sweating, with possible cardiac complications, such as heart failure,
tachycardia or atrial fibrillation. It must be taken into consideration that in the elderly the clinical manifestation of hyperthyroidism is often atypical and can easily be attributed to other medical conditions. In elder patients signs and symptoms of thyreotoxicosis are frequently related to cardiovascular, gastrointestinal and neuropsychiatric disorders. Most often there is an occurrence of atrial fibrillation, worsening of cardiac failure and angina pectoris, weight loss, anorexia, constipation and cognitive impairment.

A thyroid associated ophthalmopathy is also possible in MLS, but rare.

In our 28 cases of MLS only 2 patients (7%) presented a Graves ophthalmopathy.

**Imaging findings OR Procedure details**

**Laboratory tests/examinations**

- TSH (Thyroid Stimulating Hormone): suppressed (usually <0.01 mU/l).
- Thyroid hormones FT3 and FT4: increased or in the upper limit (manifest or subclinical hyperthyroidism) (amount depending of test-levels).
- TSH receptor antibodies (TRAb): increased in >80%.

**Imaging findings**

**Scintigraphy**

- In Graves disease Tc-99m pertechnetate or iodine-123 (for diagnostic) or iodine-131 (for quantification of uptake for planning radiodine therapy) thyroid scan shows homogenously increased activity throughout the gland with high target-to-background levels (Fig. 1).
- In toxic adenoma the scan shows a single hot nodule with no activity in the rest of the gland (Fig. 2).
- In MLS the scan shows a diffuse increased uptake of the thyroid but also one (or more areas) of focal activity (hot nodules) (Figs, 3-8).
Technetium uptake (TcTU) is increased (2-10%). The radioactive iodine uptake (RAIU) is usually greater than 40% in patients with MLS.

A diffuse increased isotope captation with one (or more) hot nodule(s) and with iodine-131-uptake greater than 50% allows the scintigraphic diagnosis of MLS.

**Ultrasound**

In MLS grayscale US shows a normal or slight enlarged gland with one or more nodules. These nodules are usually hypoechoic or isoechoic (in about 76%), and only hyperechoic in about 24%. The mostly heterogeneous nodules with halo have usually cystic and solid components. (Figs. 9,13,17,19,21,25,30). On Color Doppler the nodules show a predominately perinodular vascularity (Figs. 10,13,18,20,22,26,27,29). Additional central vascularization of the nodules in MLS is also possible (Fig. 31).

The rest of the thyroid presents in grayscale US a hypoechoic, heterogeneous spotty parenchymal echo pattern (Figs. 11,14,15,23) with marked increased vascularity in Color Doppler. (Figs. 12,14,16,24,29,32).

**Treatment**

2. Beta blockers: Propranolol.
3. When an euthyroid state or, at least, a subclinical hyperthyroidism is reached, a definitive management of MLS must be performed: Surgery or radiodine therapy.

Radioiodine is considered the definitive treatment of choice in patients with MLS. In our collective, 25/28 patients underwent one I-131-Therapy, with success in 92%. Only 2/25 Patients needed a second radiodine therapy. After that the hyperthyroidism was also eliminated. That means that with 1-2 radiodine therapies a successful definitive management of MLS can be obtained.
Fig. 1: Thyroid scan with technetium-99m pertechnetate shows the typical diffuse increased concentration of radionuclide in Graves disease. The uptake is uniform and no nodules are visualized. Technetium-99m Uptake (TcTU): 3.6%. Anti-thyrotropin receptor antibody (TRAb): 12.5 IE/l.
Fig. 2: Thyroid scintigraphy detects a focal area of increased radionuclide concentration in the right lobe with suppression of remaining thyroid tissue. Only the "hot" nodule is visualized on the scan.
Fig. 3: Thyroid scintigraphy with Tc-99m pertechnetate. Typical diffuse increased uptake for Graves’ disease with high target-to-background levels, but with additional focal area of increased concentration of radionuclide in the middle portion of the right lobe. TcTU: 4,2%. TRAb: 7,5 IU/l. (Case 1 MLS. Corresponding ultrasound: Figs. 9-12).
Fig. 4: Patient with hyperthyroidism. Thyroid scan shows a "hot" nodule in the lower left lobe with diffuse increased uptake in the right lobe. TRAb: 28 IU/l. (Case 2 MLS. Corresponding ultrasound: Figs.13-14).
Fig. 5: Thyroid scan showing diffuse uptake with focal concentration of the radionuclide in the middle till the lower portion of the left lobe. Ultrasound (Figs.15-20) revealed two solid nodules with perinodular vascularity typical for autonomously functioning adenomas. TRAb: 25 IE/l. (Case 3 MLS. Corresponding US: Figs. 15-20).
Fig. 6: Thyroid scintigraphy of a patient with hyperthyroidism shows a diffuse, asymmetrical increased uptake with a focal area of increased radionuclide concentration on the medial side of the lower right lobe. TcTU: 9,3%. TRAb: 18 IU/l. (Case 4 MLS. Corresponding ultrasound: Figs.21-24).
Fig. 7: Patient with hyperthyroidism. The initial diagnosis of Graves’ disease was based on high TRAb titers. Thyroid scan shows increased, but inhomogeneous uptake with small focal areas of increased concentration of the radionuclide in both lobes. Corresponding Color Doppler Ultrasound (Figs. 25-29) revealed three thyroid nodules with perinodular vascularity, indicating the additional presence of autonomously functioning adenomas. (Case 5 MLS. Corresponding US: Figs.25-29).
**Fig. 8:** I-131-Scintigraphy performed before radiodine therapy for hyperthyroidism in a patient with MLS. The scan shows homogeneous but asymmetrical increased uptake with a focal area of increased radionuclide concentration in the middle portion of the right lobe. Thyroid radiodine uptake (RAIU): 62%. TRAb: 8,5 IU/l. (Case 6 MLS. Corresponding ultrasound: Figs.30-32).
Fig. 9: Transverse grayscale US. Hypoechoic nodule with small cysts and halo corresponding to the focal area of slight increased uptake in the right lobe on the thyroid scintigraphy. (Case 1 MLS. Corresponding thyroid scan: Fig. 3).
**Fig. 10:** Corresponding transverse Color Doppler US shows perinodular vascularity and only slight parenchymal perfusion in the nodule. (Case 1 MLS. Corresponding thyroid scan: Fig. 3).
**Fig. 11:** Longitudinal grayscale US of the contralateral left thyroid lobe. Hypoechoic, heterogeneous spotty parenchymal echo pattern. (Case 1 MLS. Corresponding thyroid scan: Fig. 3).
Fig. 12: Corresponding longitudinal Color Doppler US shows marked vascularity of the left lobe ("thyroid inferno"). (Case 1 MLS. Corresponding thyroid scan: Fig. 3).
Fig. 13: Longitudinal Color Doppler US shows a haloed hyperechoic nodule with slight perinodular perfusion corresponding to the hot nodule in the lower left lobe on the thyroid scan. Note also the marked vascularity in hypoechoic surrounding thyroid tissue. (Case 2 MLS. Corresponding thyroid scan: Fig.4).
**Fig. 14:** Transverse Color Doppler US of the contralateral right lobe. Hypoechoic echo pattern with marked vascularity. (Case 2 MLS. Corresponding thyroid scan: Fig.4).
Fig. 15: Longitudinal grayscale US shows a hypoechoic, inhomogeneous structure of the right thyroid lobe. (Case 3 MLS. Corresponding thyroid scan: Fig.5).
Fig. 16: Corresponding longitudinal Color Doppler Ultrasound. Hypervascularity of the right lobe. (Case 3 MLS. Corresponding thyroid scan: Fig.5).
Fig. 17: Longitudinal grayscale US of the contralateral lobe shows a partially haloed inhomogeneous hypoechoic nodule in the middle portion of the left lobe. (Case 3 MLS. Corresponding thyroid scan: Fig.5).
Fig. 18: Corresponding longitudinale Color Doppler US: perinodular vascularity of the nodule in the middle portion of the left lobe. (Case 3 MLS. Corresponding thyroid scan: Fig.5).
Fig. 19: Longitudinal grayscale US detects another hypoechoic nodule with small cysts and halo on the caudal side of the left thyroid lobe. (Case 3 MLS. Corresponding thyroid scan: Fig.5).
Fig. 20: Corresponding longitudinal Color Doppler US shows also perinodular vascularity in the lesion on the caudal side of the left thyroid lobe. (Case 3 MLS. Corresponding thyroid scan: Fig.5).
Fig. 21: Transverse grayscale US detects a hypoechoic nodule with cysts in the lower right lobe corresponding to the hot lesion on the thyroid scan. (Case 4 MLS. Corresponding thyroid scan: Fig.6).
Fig. 22: Corresponding transverse Color Doppler US showing perinodular vascularity and only few intranodular perfusion. (Case 4 MLS. Corresponding thyroid scan: Fig.6).

Fig. 23: Transverse grayscale US of the contralateral left lobe. Slight hypoechoic and inhomogeneous structure. (Case 4 MLS. Corresponding thyroid scan: Fig.6).
Fig. 24: Corresponding transverse Color Doppler US reveals a marked increase in vascularity of the left lobe. (Case 4 MLS. Corresponding thyroid scan: Fig.6).
Fig. 25: Transverse grayscale US of the lower right lobe shows a haloed hypoechoic nodule with small cystic components. (Case 5 MLS. Corresponding thyroid scan: Fig.7).
Fig. 26: Longitudinal Color Doppler US shows perinodular perfusion of the nodule and marked vascularity in hypoechoic surrounding parenchyma of the right lobe. (Case 5 MLS. Corresponding thyroid scan: Fig.7).
**Fig. 27:** Longitudinal Color Doppler US of the lower left lobe detects a inhomogeneous hypoechoic nodule with halo and perinodular vascularity corresponding to the slight focal uptake on thyroid scan. (Case 5 MLS. Corresponding thyroid scan: Fig.7).
**Fig. 28:** Grayscale US reveals a another hypoechoic lesion in middle portion of the left lobe (third autonomously functioning nodule). (Case 5 MLS. Corresponding thyroid scan: Fig.7).
Fig. 29: Corresponding longitudinal Color Doppler US of the middle portion of the left lobe. Perinodular vascularity in the nodule. Note also the marked vascularity in hypoechoic surrounding thyroid tissue. (Case 5 MLS. Corresponding thyroid scan: Fig.7).
**Fig. 30:** Transverse grayscale US shows a haloed hypoechoic nodule with cysts and small calcifications corresponding to the hot nodule in the right lobe on the thyroid scan. (Case 6 MLS. Corresponding thyroid scan: Fig 8).
Fig. 31: Corresponding transverse Color Doppler US. Marked perinodular vascularity and additional internal perfusion of the nodule in the right lobe. (Case 6 MLS. Corresponding thyroid scan: Fig 8).
Fig. 32: Transverse Color Doppler US of the contralateral left lobe shows a marked increase in vascularity. (Case 6 MLS. Corresponding thyroid scan: Fig 8).
**Conclusion**

Physicians, especially general practitioners, endocrinologists, nuclear medicine specialists, radiologists and surgeons must know the possible existence of this syndrome in patients with hyperthyroidism. Careful interpretation of thyroid scan is needed, especially in patients previously diagnosed as Graves disease. In association with the scintigraphic appearance and elevated TSH receptor antibodies, Color Doppler US allows the definitive diagnosis of Marine-Lenhart Syndrome.

**Images for this section:**
**Fig. 1:** Patient with hyperthyroidism. The initial diagnosis was Graves’ disease based on high TRAb titers. However, the thyroid scan showed an asymmetrical thyroid enlargement with diffuse, but asymmetrical increased uptake, especially in a focal area of the lower left lobe.
Fig. 2: Longitudinal grayscale US of the enlarged left lobe. Haloed hyperechoic nodule with central hypoechoic to liquid lesion in the lower left lobe, corresponding to the focal concentration of radionuclide on the thyroid scan. The rest of the left lobe shows a hypoechoic, heterogeneous spotty echo pattern.
**Fig. 3:** Corresponding transverse Color Doppler shows a perinodular vascularity of the nodule in the lower left lobe.
Fig. 4: Color Doppler US of the upper left lobe. Marked vascularity of the hypoechoic thyroid parenchyma above the nodule.
Fig. 5: Longitudinal Color Doppler US of the contralateral right lobe. Marked vascularity ("thyroid inferno", typical for Graves’ disease) in hypoechoic thyroid tissue.
References