Marine-Lenhart Syndrome: A Case Report
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Citation

Abstract
The association of Graves's disease with toxic nodules constitutes Marine Lenhart syndrome. It is a rare pathology with prevalence between 2.7 and 4.1%. Its physiopathology remains complicated incriminating antithyroidian autoantibodies such as TSH antireceptors autoantibodies.

The treatment by the iodine 131 could be an activating factor. The thyroid scintigraphy by the iodine 123 or by the pertechnetate shows a diffuse increased uptake without suppression of the remainder of the gland and with focused raising nodular activity.

This paper presents a case report of Marine-Lenhart syndrome and a discussion of the association of Graves's disease with thyroid nodules as well as the therapeutic approach, through a review of the literature.

INTRODUCTION
Graves's disease is an autoimmune pathology. It can be suspected through the analysis of the histology, which shows the infiltration of the thyroid, by lymphocytes and plasmocytes. It can also be suspected through biological disorder, revealing thyroid-stimulating immunoglobulin (TSI). The TSH antireceptors autoantibodies -only measured in routine- play an important role in the activation of the glandular function, which leads to hyperthyroidism.

The association of thyroid nodules with Graves's disease is found in 25 % to 30 % ($\gamma_1$, $\gamma_2$) of patients affected by Graves's disease. More than 95 % of these nodules are hypoactive and a small percentage is hyperactive. Therefore, these patients are candidates for thyrotoxicoses due to the Graves's disease and to the toxic nodule. These patients present Marine-Lenhart syndrome ($\gamma_3$, $\gamma_4$).

We present a case report of Marine-Lenhart syndrome and we discuss the physiopathology approach and the therapeutics of this syndrome through a literature review.

CLINICAL CASE
85-year-old patient was admitted in the nuclear medicine department in April 2005 for the iodine 131 therapy of a fruste hyperthyroid known for 2 years. Clinically, the patient reported asthenia, thermophobia and insomnia. The palpation of the neck found a nodule in the left thyroid lobe. Biologically, TSHus was 0.11 uUI/l, T3L, T4L were normal, and the anti receptors of the TSH were positive. The scintigraphy by the iodine 123 (figure 1) showed a voluminous toxic nodule in the base of the left lobe without suppression of the remainder parenchyma and with an uptake at 2 hour of 7 %. The thyroid ultrasonography showed two nodules in the base of the left lobe measuring 35 and 18 mm. A radiiodine treatment (20 mCi) was delivered on April 29, 2005. The treatment by NeoMercazole was quickly stopped because of an allergy.

A clinical (thermophobia, tachycardia, diarrhea, discrete exophthalmia) and biological (TSH: 0.01; LT4: 37.9; LT3: 10.6 and TSI: 39.8) hyperthyroidism had appeared. The ultrasonography objectified a 6 centimeters subtotal left nodule. The thyroid scintigraphy showed a voluminous toxic nodule without contralateral suppression, the uptake was 17 % at 2 hours. The basdene test was stopped for allergic reason. Towards the end of August 2005, the patient was hospitalized and propylthiouracil was prescribed at the rate of eight tablets a day.
DISCUSSION

The association of the thyroid nodules with the Graves's disease is present among 25 to 30% of patients with Graves's disease. This is illustrated by studies carried out among patients operated on for Graves's disease (table 1) and among patients who were not operated (table 2).

Table 1: Studies carried out among patients operated on for Graves's disease (, , )

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Nodules in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamata Hernandez and al.</td>
<td>153</td>
<td>28.1</td>
</tr>
<tr>
<td>Mishra and al.</td>
<td>130</td>
<td>26.9</td>
</tr>
<tr>
<td>Karras and al.</td>
<td>557</td>
<td>25.1</td>
</tr>
</tbody>
</table>

The cold nodules represent the biggest percentage. In the study of Carnell and al. (6), among 60 patients having nodules:

- 27 patients: unique cold nodule 5.8%
- 21 patients: several cold nodules 4.5%
- 4 patients: hot nodules 1%

Figure 3

Table 2: Studies carried out among patients who were not operated (, )

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Nodules in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnell and al.</td>
<td>468</td>
<td>12.8</td>
</tr>
<tr>
<td>Cantalamessa and al.</td>
<td>315</td>
<td>35.7</td>
</tr>
</tbody>
</table>

The association of Graves's disease with one or several toxic nodules is the Marine-Lenhart syndrome. It is a rare syndrome with prevalence between 2.7 and 4.1% (9, 10). It can involve toxic nodule and Graves's disease simultaneously or successively. Its physiopathology remains misunderstood. We incriminate genetic alterations of the TSH receptors and the presence of TSH antireceptors autoantibodies in the development of the Marine-Lenhart syndrome in patients affected by the Graves's disease.

The treatment by iodine 131 could be an activating factor. Waldherr (11) published a case where two toxic nodules appear 13 years after the treatment by iodine of a Graves's disease. The study of Nygaard (12) among 149 patients treated by iodine for toxic nodules, showed 17 relapses after 3-6 months, among which 12 presented positive TSH antireceptors.

The scintigraphic aspect enables the distinction between Marine-Lenhart syndrome and multi hetero nodular toxic goiter. This later one presents a nodular hyperactivity with suppression of the remainder of parenchyma. While, Marine-Lenhart syndrome presents a diffuse hyperactivity with focused raising of the nodular activity.

These nodules must be well investigated to optimize the therapeutic management. The antithyroid drugs are the treatment of the choice. The treatment by the iodine 131 is to be recommended in the second place. In the case of multiple nodules, the surgical treatment is more suitable.

CONCLUSION

The clinician and the nuclear physician must be careful in the interpretation of a thyroid scintigraphy of a Graves's disease. The resistance to high doses of antithyroidian or the recurrence after their stop has to draw the attention towards the Marine-Lenhart syndrome. The evaluation of these toxic nodules is very important for optimizing the therapeutic management.

REFERENCES

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