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CASE REPORT

Paraneoplastic hyperthyroidism secondary to metastatic choriocarcinoma. Clinical Case Report.

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Abstract

Rarely, thyrotoxicosis may arise as a paraneoplastic syndrome, as in the case of choriocarcinoma. Similarities in biological structures between serum human chorionic gonadotropin (HCG) and thyroid stimulating hormone (TSH) allow HCG to exert its effects on the TSH receptor on thyroid membranes. Thyrotoxicosis was presented in a 25-year-old female patient who previously presented deterioration of alertness, intracranial hypertension, with subsequent finding of multiple metastatic lesions, with concentrations of human chorionic gonadotropin up to 500,000 mIU/mL. With adequate evolution after initiation of antithyroid and chemotherapy.

Objective

To report a case of rare pathology and review the literature to know the right approach to a case of paraneoplastic hyperthyroidism.

Keywords: Hyperthyroidism, Choriocarcinoma, Metastasis

Introduction

Thyrotoxicosis is characterized by the exposure of tissues to excessive amounts of thyroid hormone.[1] The incidence of clinical hyperthyroidism has been reported to be 0.8/1,000 women per year and is less common in men. Causes of thyrotoxicosis include Graves' disease, toxic multinodular goiter, toxic adenoma, and thyroiditis. Rarely, thyrotoxicosis may arise as a paraneoplastic syndrome.[2,3]

Historically, the first patient with clinical hyperthyroidism and choriocarcinoma is described by

Myers in 1961. Subsequently, Cohen and Utiga described that the use of chemotherapy decreased thyroid hormone concentrations.[4]

There is evidence of an association between serum human chorionic gonadotropin (HCG) concentrations and suppressed thyroid-stimulating hormone (TSH), rarely related to gestational neoplasms and other germ cell malignancies in which HCG[5] is secreted, such as choriocarcinoma.

The pathophysiology of the association is that human chorionic gonadotropin is composed of a common alpha subunit and a specific beta subunit, associated in a non-covalent way that is common to thyroid-stimulating hormone. The similarities in biological structures between HCG and TSH allow HCG to exert its effects on the TSH receptor in thyroid membranes.[6,7] Previous studies have shown that a concentration greater than 50,000 IU/l is associated with TSH suppression and clinical hyperthyroidism.[8] The stimulatory HCG effect is relatively weak, since for every 10,000 IU/L increase in HCG concentrations, T4L increases on average by 0.6 pmol/L, with a decrease in TSH of 0.1 mU/I.[9]

Next, a description of the clinical case is made.

A 25-year-old female with no history of disease: cesarean section twice 8 and 4 years ago without later complications, abnormal uterine bleeding of 3 years of evolution of unidentified etiology. Other pathologies are denied. He began suffering 5 months prior to admission, progressive holocranial headache, oppressive type treated with analgesics without improvement, after admitted to the emergency unit due to deterioration of alertness, with clinical data of intracranial hypertension. It was assessed by neurosurgery documented by simple computerized axial tomography of skull intraparenchymal hematoma, left frontal, decompressive craniectomy and biopsy of subcortical intraxial cortical lesion in left middle frontal gyrus, with report of neoplasm pathology compatible with choriocarcinoma. During its study protocol, metastatic pulmonary and hepatic lesions, metastatic left renal destruction, with total nephrectomy were documented. Therefore, an assessment is made by medical oncology, who decides to admit her for the start of chemotherapy. Clinically at admission, heart rate of 105 beats per minute stands out, arrhythmic, with a sensation of palpitations, no increase in neck volume is observed and no thyroid growth is palpable, no orbitopathy data, no neurological alterations, no tremor, thyroid storm is ruled out with a score on the Burch and Wartosfsky scale of 15 points. During its assessment upon admission, a thyroid profile and general laboratories are performed, biochemically compatible with hyperthyroidism.

Table 1. Biochemical profile of the patient

Leukocytes	11.5 K/ul
Hemoglobin	8.9 gr
Hematocrit	26.7 %
Platelets	341 x 10 3
Glucose	103 mg/dL
Urea	25.68 mg/dL
Creatinine	0.57 mg/dL
Sodium	136 mmol
Potassium	4.7 mmol
Magnesium	2.0 mg
Alkaline phosphatase	205UI/L
Lactate dehydrogenase	665UI/L

Table 2. Thyroid profile of the patient

Hormone	Unit of measurement	Basal	1stChemotherapy cycle	2ndChemotherapy cycle	3rdChemotherapy cycle
TSH	µUI/mL	0.0	0.01	0.34	0.82
T4 free	ng/dL	2.16	1.97	1.14	0.93
T4 total	µg/dL	24.86	16.89	9.44	9.82
T3 free	pmol/L	20.88	5.3	3.1	3.9
T3 total	ng/dL	335.01	172.5	89.62	65.71
GCH beta	mUI/mL	500, 000	86,564	1,110	1,457

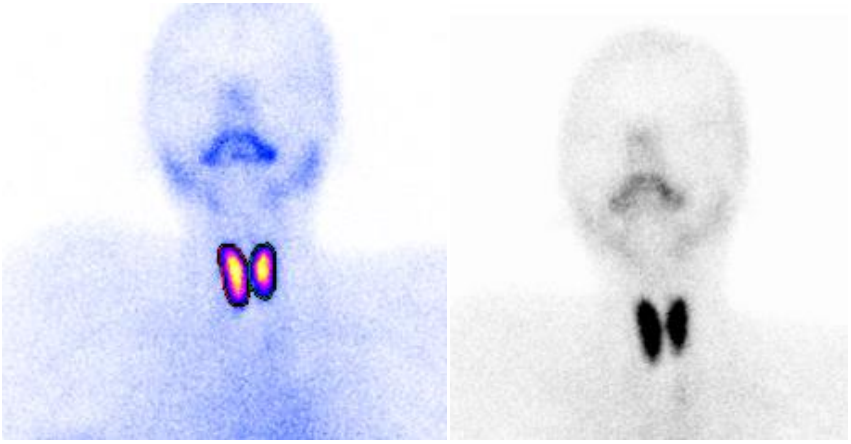

Figure 1. Thyroid gamma gram with 99m TcO4 and percentage of uptake 370 MBq. Qualitative data are seen in relation to thyroid hyperfunction without goiter.

During his hospitalization, due to the first clinical and biochemical characteristics, the diagnostic conclusion was reached of paraneoplastic hyperthyroidism associated with elevated levels of HCG. Treatment was started with thiamazole titrated to T4L levels; 5 mg orally every 8 hours, beta blockade was added with propranolol at a dose of 40 mg orally every 12 hours, cardiology assessment confirming paroxysmal atrial fibrillation.

Oncology initiation of chemotherapeutic treatment based on etoposide 140 mg intravenously daily for 3 days and cisplatin 25 mg intravenously daily for 3 days in three cycles.

He reported clinical improvement 6 days after starting treatment, with a decrease in the sensation of palpitations and tremor. After the first cycle of chemotherapy, thyroid profile control is performed.

Discussion

The prevalence of hyperthyroidism in patients presenting with metastatic no seminoma germ cell tumors is currently unknown; however, in a large prospective cohort analysis study of 144 patients, Oosting et al, hyperthyroidism was identified as present in 3.5% of patients with disseminated no seminoma germ cell tumors. In patients with elevated serum levels of HCG (> 50 000 IU / l), a prevalence of hyperthyroidism of 50% was found10. As in the case presented, the concentrations were 500, 000 mIU/mL with prospective thyrotoxicosis. Patients with CGH-induced hyperthyroidism have suppressed TSH levels and elevated free thyroid hormones, but usually lack the clinical features of Graves' disease and TSH11 receptor antibodies. Clinically choriocarcinoma presents a rapid invasion, widely malignant metastases. The preferred sites of involvement are the lungs (94% of metastatic GCCs) and the vagina (44%), followed in descending order of frequency by the liver (28%) and brain (28%).[12] Brain metastases are seen in decreasing order of frequency from the parietal lobe to the temporal to the frontal lobes, presenting intracranial hemorrhage as the most frequent mode of presentation of brain involvement and stands for two thirds of brain metastases.[13] Brain involvement is usually seen in patients with advanced disease; Virtually all patients with brain metastases have concurrent lung or vaginal involvement or both. It is exceedingly rare for such lesions to arise in the absence of lung metastases.[14]

Likewise, the treatment of paraneoplastic hyperthyroidism should be treated immediately with β-adrenergic receptor antagonists and antithyroid drugs for better tolerability of chemotherapy.[15]

The treatment of choriocarcinoma with brain metastases involves chemotherapy in conjunction with cranial irradiation16. Initiation of chemotherapy in patients with paraneoplastic hyperthyroidism results in a rapid decrease in HCG and T4 L. HCG has a half-life of 18 to 36 h, but initiation of chemotherapy may initially result in a sudden increase in tumor markers.[17] In theory this can aggravate hyperthyroidism and cause a thyroid storm, so close monitoring should be taken, however, this should not delay the start of chemotherapy. As described in the literature, the clinical and biochemical evolution of the patient was initially adequate with the use of antithyroid drugs and beta-blockers, however, the initiation of chemotherapy treatment should be prioritized as a cornerstone of curative treatment of thyrotoxicosis.

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Conflicts of Interest

None

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