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Unusual etiology of secondary thyrotoxicosis and its presentation

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Dear Editor,

The incidence of clinical hyperthyroidism has been reported as 0.8/1,000 women per year, and it is less common in men.[1] Causes of thyrotoxicosis include Grave's disease, toxic multinodular goiter, toxic adenoma, and thyroiditis. Rarely, thyrotoxicosis can arise as a paraneoplastic syndrome. In this setting, systemic symptoms of underlying malignancy may be wrongly attributed to primary hyperthyroidism leading to a delay in diagnosis.[2] We report a rare case of thyrotoxicosis due to metastatic nonseminomatous germ cell tumor (NSGCT) of testis that highlights the importance of a systematic clinical and biochemical assessment.

A 48-year-old man presented with persistent gradual back pain for 2 months with inconclusive magnetic resonance imaging (MRI) findings, so lumbar spondylitis was assumed and started on symptomatic treatment. On laboratory results, patient showing primary hyperthyroidism (triiodothyronine (T3) 14.2 ng/dL, thyroxin (T4) 138 μg/dL, and thyroid stimulating hormone (TSH) 0.14 μIU/mL) was treated with radioiodine thyroid ablation in absence of

hyperthyroidism signs and symptoms based upon enhanced diffuse thyroid tracer uptake on thyroid scan mimicking Grave's disease.

On appearance of palpable supraclavicular lymph node, palpable mass in the left upper abdominal quadrant and enlarged right side testis with secondary hydrocele were detected on systemic examination, which were probably missed on initial evaluation. Fine needle aspiration cytology of supraclavicular lymph node showed a germ cell tumor. Human chorionic gonadotropin (HCG; 57,220 mIU/L), alfa fetoprotein (193 U/L), and lactate dehydrogenase (777 U/L) were markedly elevated. Final diagnosis of carcinoma testis, NSGCT, stage III C, poor prognosis risk group with paraneoplastic hyperthyroidism was arrived upon and started upon two cycles of PEB (cisplatin, etoposide, bleomycin) chemotherapy. Patient underwent high inguinal right side orchiectomy after two cycles of PEB chemotherapy, and on histopathological examination, presence of mixed germ cell tumor with predominantly teratoma (90%) and choriocarcinoma (5%) elements was diagnosed. His tumor marker values were decreased on chemotherapy with recovery of thyroid function with thyroxin supplementation [Table 1]. Two more cycles of PEB chemotherapy with surgical excision of residual disease was planned.

Paraneoplastic hyperthyroidism is a rare but recognized phenomenon associated with NSGCT and high-serum HCG levels, although the exact prevalence is unknown. In one large prospective cohort analysis study of 144 patients, Oosting *et al*., reported hyperthyroidism to be present in 3.5% of the patients with disseminated NSGCT and almost 50% in patients with high-serum HCG levels (>50,000 IU/L).[3] Exceedingly high concentration of HCG in occasional germ cell tumors can overcome its low-binding affinity of the alpha subunit for TSH receptor for inducing secondary hyperthyroidism. There is lag time between elevated thyroid hormone levels and clinical evidence of hyperthyroidism.[4] Despite lack of standard guidelines for management of paraneoplastic hyperthyroidism, symptomatic hyperthyroidism should be treated immediately with β-adrenergic receptor antagonist and antithyroid drugs for better tolerability of chemotherapy.[3,5,6] The treatment of the underlying cancer is definitive treatment of paraneoplastic hyperthyroidism. In conclusion, this case highlights the importance of a comprehensive clinical history and systematic physical examination including genitals for all patients presenting with hyperthyroidism.

Table 1: Serial tumor markers showing progressive decline in their levels in response to chemotherapy and orchiectomy

	Baseline 1st PEB	2nd PEB	Post orchiectomy
AFP	4,000	193	63
Beta HCG	57,220	10,000	1,000
LDH	700	Normal	Normal

PEB=Cisplatin, etoposide, bleomycin, AFP=alpha fetoprotein, HCG=human chorionic gonadotropin, LDH=lactate dehydrogenase

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Consent

Written informed consent was obtained from the subject for publishing this case report and accompanying images.

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