

Case presentation

Amouzegar,A MD

Associate professor

Endocrine Research Center, Research Institute For Endocrine Sciences,
Shahid Beheshti University, Tehran

Case 1:

- A 41-year-old man presented with a chief complaint of fainting during exercise
- No history of fatigue, weight gain, or constipation
- TSH was 437 $\mu\text{IU/mL}$ (0.5–5.5 $\mu\text{IU/mL}$)
- Repeated 2 days later, TSH was 302 $\mu\text{IU/mL}$
- Free T4 and total T3 were unremarkable, 0.9 ng/dL (0.8–1.7 ng/dL) and 87 ng/dL (50–170 ng/dL), respectively

What do you recommend?

- The TSH value suggests hypothyroidism or secondary hyperthyroidism
- Neither is consistent with the history, free T4, or total T3

TSH was tested on 5 different assays

Table 1.

Undiluted and diluted TSH results ($\mu\text{IU/mL}$) on 5 TSH assays from 4 manufacturers.

	Siemens Centaur TSH3-UL	Siemens Centaur TSH	Abbott Architect TSH	Beckman Coulter Dxl TSH	Roche Elecsys TSH
Undiluted	>150	7	8	68	301
$\times 10$	366	63	100	142	275
$\times 100$	407	193	246	245	323
$\times 1000$	373	225	295	350	–

TSH, thyroid-stimulating hormone.

Case 2

- A 45-year-old man presented with severe hyperthyroidism
- Serum Total T4 was 22 mcg/dl (reference range 4-12 mcg/dl), FT3 >25.0 pg/mL (reference range 1.7 to 3.7 pg/mL)
- Thyroid scintigraphy revealed diffuse and increased uptake, and thyroid ultrasound and color flow Doppler imaging showed typical findings of Graves' hyperthyroidism
- Tested positive for thyroid receptor Antibody (TRAb) on second-generation test that was 3.1 IU/L (reference range <1.0 IU/L)

Cont

- Within 9 months of treatment with oral MMI (20 mg/day), TRAb titers had normalized, but he experienced sustained hyperthyroidism for more than 8 years, requiring 15 mg/day of MMI to correct hyperthyroidism

Questions

- TRAb (stimulatory / inhibitory/ blocking)?
- The second or third generation?
- Reference limit Vs high titers
- Role in diagnosis?

Case 3

- A 36-year-old woman was seen in follow-up for further management of PTC
- She initially presented with a right lobe thyroid nodule
- FNA revealed a follicular neoplasm, and she underwent a right hemithyroidectomy that revealed a 4.6-cm follicular variant of PTC with perivascular lymphatic invasion and lymphocytic thyroiditis
- She had completion thyroidectomy that revealed lymphocytic thyroiditis and was then treated with 150 mCi of I-131 therapy after levothyroxine (L-T4) withdrawal
- Anti-Tg antibodies were elevated at the time of treatment, and Tg levels were undetectable
- Post-therapy whole body radioiodine scans revealed uptake in the thyroid bed with no evidence of regional or distant metastases

Cont

- The patient was placed on TSH-suppressive doses of L-T4 and was monitored thereafter with a combination of neck ultrasound, TSH, Tg, and anti-Tg antibody levels with persistently positive anti-Tg antibodies
- She also had a 4-mCi, I-131 whole body scan after L-T4 withdrawal with no uptake
- The Tg and anti-Tg antibody measurements have been performed in the *same laboratory using a single assay system* (Immulite 2000 and L2KTG, respectively; Siemens, Deerfield, Illinois)
- Tg levels have been measured yearly and have been persistently undetectable

Cont

- The anti-Tg antibody levels are as follows
- Yearly Abs titers were 159; 162; 152; 74; 53, 37.6 (reference range, <40; lower limit of detection, <20 (IU/ml)

Cont

- Neck Us was performed periodically without evidence of disease
- Chest CT scans without iv contrast twice revealed 2 stable tiny lung nodules that were not felt to be consistent with metastases.
- Thus, at this time the patient has dropping anti-Tg antibodies and no certain radiographic or functional evidence of residual thyroid cancer

Case4

- 63-year-old man had undergone subtotal thyroidectomy for a thyroid nodular lesion in, with negative anti-TPOAb
- After the diagnosis of PTC (T2N1M0), a total thyroidectomy was performed followed by radioiodine ablation with 100 mCi ¹³¹I
- Post-therapy WBS showed only cervical uptake
- Stimulated serum Tg obtained after thyroxine withdrawal (TSH = 73.9 UI/L) was 0.65 ng/mL
- Serum Tg measurement was done using a commercial immunometric (IMA) chemoluminescence assay with *analytic sensitivity of 0.2 ng/mL, functional of 0.9 ng/mL*, inter- and intrassay variability less than 8.8% and 6%, respectively, and normal reference values of 1.60 - 60 ng/mL

Cont

- *Commercial* anti-Tg autoantibody assay (chemoluminescence) had analytic sensitivity of 10 IU/mL, functional of 20 UI/mL, interassay and intrassay variability less than 9.1% and 3.9%, respectively, and normal values < 40 UI/mL

Cont

- Serum thyroglobulin was undetectable during suppressive TSH therapy, while serum anti-thyroglobulin antibodies were elevated (681 U/mL)
- Extensive investigation was performed by whole body scans, cervical US, thorax and cervical CT, but the site of tumor recurrence could not be detected

Question

- What is the meaning of analytic sensitivity, functional , inter- and intrassay variability ?