



DIAGNOSTIC DILEMMA: A CASE OF UNDETECTABLE TSH



R. Mimms¹, I. Sirisena^{1,2}

¹ Department of Endocrinology, Diabetes & Metabolism, Temple University Hospital, Philadelphia, PA

² Lewis Katz School of Medicine at Temple University, Philadelphia, PA

CONTACT INFORMATION

remy.mimms@tuhs.temple.edu

Introduction

- Under steady state, measurement of TSH is accepted as the best assessment of thyroid function with current assays having very low limits of detection
- When evaluating a patient with abnormal thyroid function tests but without symptoms, an appraisal of the test should be considered

Clinical Case

- A 63-year-old South Asian man was referred to endocrinology for evaluation of non-detectable TSH on Siemen's ADVIA Centaur TSH3-UL immunoassay
- The patient was asymptomatic
- He did not take biotin supplements
- Peripheral thyroid hormone levels were normal
- Further evaluation was also negative for TSI and heterophilic antibodies (not shown)
- Thyroid uptake and scan showed uniform uptake of 5.1% and 15.1% at 2-hours and 24-hours, respectively, with no dominant nodules (Fig 1)
- Hypothalamic-pituitary hormonal testing (not shown) and MRI pituitary were both normal (Fig 2)
- When TSH testing was repeated on a separate platform, Roche's eCLIA immunoassay, detectable values were obtained

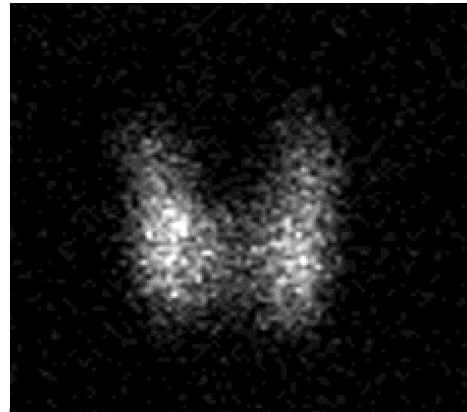


Fig 1. I-123 thyroid uptake and scan: Euthyroid gland without dominant nodules

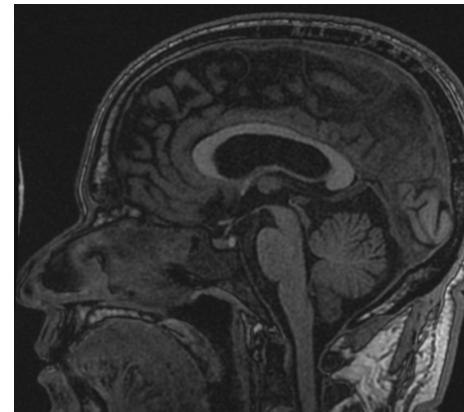


Fig 2. T1-weighted MRI in sagittal view post-contrast: unremarkable pituitary gland

Component	8.17.2017	4.24.2018	8.20.2018	11.20.2018	5.29.2019	11.4.2019
TSH (Siemens) (0.40 - 4.50 mIU/L)	<0.01 (L)	<0.01 (L)	<0.01 (L)		<0.01 (L)	
TSH (eCLIA) (0.450 - 4.50 uIU/mL)				6.48 (H)		5.79 (H)
Thyroxine, Free (0.8 - 1.8 ng/dL)	1.1	1.2		0.9	1	1.12
T4, Free, Direct Dialysis (0.9 - 2.2 ng/dL)			1.2			
T3, Total (71 - 180 ng/dL)		105	100			115
TSI (<140 % baseline)		121				

Discussion

- Testing of serum TSH by immunoassays is based on the sandwich method in which one antibody binds to the β -subunit of TSH and the other to the α - β interface
- Immunoassay tests are prone to interferences, particularly by way of altering measurable concentration of analyte or by altering antibody binding¹
- In this case, the presence of detectable TSH depended on the platform by which it was measured
- This finding suggests a TSH- β variant with impaired immunoreactivity but normal bioactivity
- Such a mutation has been previously reported to occur five times more frequently among South Asian individuals than the general population²
- Genetic testing was offered but was declined
- It is incumbent on the clinician to reconcile a test result that is discordant with the clinical presentation
- Failing to recognize a possible interference can lead to unnecessary healthcare expenditures, misdiagnosis, and inappropriate management

References

1. Favresse J et al. *Endocr Rev.* 2018;39(5):830-850
2. Pappa T et al. *Thyroid.* 2015 Aug;25(8):869-76