A case of undetectable thyroid hormones

Hayes S[1], Hawkins L[1], Halsall D[2], Joshi S[1]

[1] Biochemistry, Maidstone and Tunbridge Wells NHS Trust (MTW) , [2] Biochemistry, Addenbrooke's Hospital, Cambridge

Introduction

Positive interference in free thyroxine (fT4) and free triiodothyronine (fT3) assays is well known. However, negative interference in free thyroid hormone assays in the paediatric population is very rare. We report the case of a 3 year old girl with negative interference in the Roche method for fT4 and fT3.

Case presentation

- 3 year old girl with increasing tiredness , abdominal pain , pain in lower limbs, constipation
- No family history of thyroid disease
- Nil medication
- Clinically euthyroid
- No goitre
- Normal milestones

Results

Results	TSH (mU/L)	Free T4 (pmol/L)	Free T3 (pmol/L)
MTW (Roche)	**1.8** (0.85-6.50)	**<3.0** (12.1 – 22)	**<1.5** (3 – 9.1)

Results confirmed on repeat

9am Cortisol = 332 nmol/L

Prolactin = 154 mIU/L

IGF1 = 7.7 nmol/L (4.4 - 22.3)

Thyroid peroxidase antibodies = Negative

MRI = Normal

Short Synacthen test

0 min = 297 nmol/L

30 min = 1132 nmol/L

60 min = 1330 nmol/L

Investigating assay interference

Results	TSH (mU/L)	Free T4 (pmol/L)	Free T3 (pmol/L)
Roche	1.8 (0.85-6.50)	< 3.0 (12.1 – 22)	<1.5 (3 – 9.1)
Abbott	Insufficient	18 (9-19)	Insufficient
Centuar	2.25 (0.35 -5.5)	14.8 (10.3-22.7)	5.8 (3.5 – 6.5)
Perkin Elmer	2.68 (0.4 – 4.0)	12.7 (9 – 20)	-
Cambridge (calculated)	-	15.0 pmol/L	-

Assay differences

Results	fT4 and fT3 methods	Assay
MTW (Roche)	1 step competitive	No wash step
William Harvey (Abbott)	2 step	Wash step
Medway (Centuar)	1 step competitive	No wash step
Cambridge (Perkin Elmer)	2 step	Wash step
Cambridge (calculated)	Indirect - calculated from total T4 and TBG	

Discussion

The biochemical pattern of normal/ low TSH levels with low fT4 levels may be associated with non-thyroidal illness, pregnancy, drugs and rarely central hypothyroidism (CH) or assay interference.

CH is often accompanied by combined pituitary hormone deficiencies. Isolated congenital CH is rare and mainly due to TSHβ- subunit and thyrotropin releasing hormone receptor (TRHR) gene mutations. The spectrum of clinical features includes lethargy, short stature to severe impairment in neurodevelopment [1] . Indeed, some patients with TRHR may be asymptomatic [2].

Interference in immunoassays for TSH, fT4 and fT3 is uncommon but well known. The nature of interference may be variable in different assays due to differing assay designs. Causes include heterophilic antibodies, autoantibodies, human anti animal antibodies and abnormal binding proteins. In certain electrochemiluminescent assays, antiruthenium antibodies may account for interference[3]. Whilst there are several reports of assay interference causing falsely elevated thyroid hormone levels, reports of spuriously low levels are rare[4]. The Roche assay is a one-step competitive assay, thus is more susceptible to interference due to the aforementioned causes.

Conclusion

This case emphasizes the need for vigilance in interpreting extremely unusual immunoassay results, even if clinically plausible.

References

1. Bonomi M, Proverbio MC, Weber G, Chiumello G, Beck-Peccoz P & Persani L 2001 Hyperplastic pituitary gland, high serum glycoprotein hormone a-subunit, and variable circulating thyrotropin (TSH) levels as hallmark of central hypothyroidism due to mutations of the TSH b gene. Journal of Clinical Endocrinology and Metabolism 86 1600–1604.
2. Bonomi M, Busnelli M, Beck-Peccoz P, Costanzo D, Antonica F, Dolci C, Pilotta A, Buzi F, Persani L. A family with complete resistance to thyrotropin-releasing hormone. N Engl J Med. 2009 Feb 12;360(7):731-4
3. Zaninotto M, Tognon C, Venturini R, Betterle C, Plebani M. Interference in thyroid hormones with Roche immunoassays: an unfinished story. Clin Chem Lab Med. 2014 Dec;52(12):e269-70.
4. Stehouwer MH, Stehouwer CD, Hackeng WH. Falsely low serum thyroxine levels caused by interference with the thyroxine assay. Neth J Med. 1991 Aug;39(1-2):20-2.

Thyroid 110-EP

mtw.nhs.uk
Maidstone and Tunbridge Wells Hospitals

BES2016 110--EP

Thyroid

Samantha Hayes

DOI: 10.3252/pso.eu.BES2016.2016

Poster presented at: SfE BES 2016 7-9 November BRIGHTON

PosterSessionOnline.com