

A Case of False Positive Macro-prolactin

Sir,

A 31-year, non-smoker, Caucasian lady was referred by her general practitioner (GP) to Endocrinology Clinic with hyperprolactinaemia. She denied galactorrhoea, irregular periods and visual problems. She complained of headaches for previous 10 years with increase in frequency recently. She denied clinical features of other pituitary hormones' excess or deficiency. She was receiving treatment for acne for previous few years from her dermatologist. She used doxycycline for six months last year and was now using isotretinoin for a few months for the same. She noticed significant clinical improvement in her acne. Her mother had type 2 diabetes and paternal uncle had essential hypertension. She was allergic to penicillin. On examination, her vital signs were within normal ranges, visual fields were full on confrontation method and no neurological signs were detected. Laboratory investigations showed normal pituitary profile except high total prolactin, 2055 mIU/L (Normal range: 102-496 mIU/L) and a positive macro-prolactin screen using polyethylene glycol (PEG) with bioactive prolactin, 332 mIU/L (<350 mIU/L). Since the bioactive prolactin was within normal range and she was asymptomatic, no treatment was required, so was discharged from clinic back to her GP care.

Table 1:

	Time 0	15 months	17 months	18 months
Prolactin (mIU/L)	2055 PEG*	2017 PEG	1913 PEG	3025 Gel filtration
Macroprolactin/ bioactive	Predominantly macroprolactin	Predominantly bioactive	Predominantly bioactive	Predominantly bioactive
LH (IU/L)	1.1		1.2	
FSH (IU/L)	2.6		2.3	
TSH (0.27-4.27 mIU/L)	3.45		2.94	
FT ₄ (12-22 pmol/L)	11.6		12.3	
Cortisol (176-536 nmol/L)	218		438	
Oestradiol (Follicular phase 45 - 854, Ovulatory phase 151 - 1461, Luteal phase 82 - 1251)	468		426	
IGF-1 (15-42 nmol/L)	25.6		18.1	

PEG*: Polyethylene glycol.

About 12 months later, her GP repeated her blood tests including prolactin levels. Her total prolactin remained high at 2017 mIU/L with minimal macro-prolactin detected using PEG. The test was repeated a month later, which once again had bioactive prolactin of 1913 mIU/L (Table I). We then performed the test using gel filtration, which confirmed total prolactin of 3025 mIU/L, predominantly bioactive. Going through her history, she discontinued

isotretinoin about nine months ago. There was no other change compared to a year ago, when her first prolactin level was measured. Her pituitary MRI scan detected a micro-prolactinoma of 4 mm and was then treated with cabergoline, as she was planning to conceive. Her prolactin responded well to this treatment and started to settle.

Macro-prolactin, also called "big-big" prolactin, is formed by prolactin-immunoglobulin complexes and may cause elevation of serum prolactin concentrations measured by standard assays, potentially leading to unnecessary investigations and/or treatment.¹⁻³

This case of false positive macro-prolactin most likely was due to high immunoglobulin levels with isotretinoin use for acne in a young female. Isotretinoin should be considered a possible cause of false positive macro-prolactin in selected patients with high macro-prolactin levels.

PATIENT'S CONSENT:

Informed consent was obtained from the patient to publish the data concerning this case.

CONFLICT OF INTEREST:

The author declared no conflict of interest.

AUTHOR'S CONTRIBUTION:

AIS: Responsible for all aspects of this manuscript.

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