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Case Report

Nocturnal and Diurnal Variation of Serum Prolactin in Middle-Aged Adult Female: A Unique Case Report

Suresh D.R.*, Khalida Parveen Basha*, Shabnam Roohi*

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Abstract

A 38 year old lady was admitted with history of dyspnea & paroxysmal events of variable duration. MRI Contrast of Brain performed in 2014 suggested microadenoma. She had irregular menstrual cycle & overnight video-EEG monitoring revealed complex partial seizures with secondary generalization. Serum prolactin levels at 3:41 PM were 5.27 ng/mL on the day of admission, at 4:53 AM on the next day it was 58.37 ng/mL. The repeat tests showed precision & prolactin at 12:25 PM repeat test on fresh sample was 12.48 ng/mL. The etiopathogenesis for isolated early morning peak level was thoroughly investigated and literature studies suggested nocturnal and diurnal variation with eightfold early morning peak in prolactin levels when associated with oligomenorrhea or neurological medication. This case was unique that there was an isolated eleven-fold rise in serum prolactin which is uncommon.

Keywords: Hyperprolactinemia; Nocturnal Variation; Microadenoma; Prolactin; Diurnal Variation.

Introduction

Prolactin (an anterior pituitary hormone) secretion is pulsatile and exhibits dirurnal variation owing to plenty of mediators of central, pituitary, and peripheral origin. Hyperprolactinemia, a condition of elevated prolactin levels is a common endocrine disorder of the hypothalamic-pituitary axis in blood and occurs more commonly in women. The prevalence of hyperprolactinemia ranges from 9-17% in women with reproductive diseases [1].

Case Details

A 38 year old lady who was normotensive, non-diabetic presented with complaints of dyspnea (NYHA class IV) associated with orthopnea, PND & episode of confusion last night associated with slight frothing was admitted at SAKRA World Hospital, Bangalore. History of cough with no expectoration. Patient had right sided headache associated with nausea from 1 day, loose stools about 4 episodes, watery foul smelling & no blood in stools. No history of loss of consciousness, fever, chest pain & palpitations. Patient was a known epileptic & was on Tab.Levipil 250 mg BD. Patient was also a known case of hypothyroidism on treatment. On General Physical Examination, she was afebrile, pulse was 72/min, regular, respiratory rate was 20/min & Blood Pressure was 100/60 mm Hg. Systemic examination revealed normal CVS, Respiratory & gastrointestinal functions & on CNS examination there were no neurological deficits. Multiplanar MRI Brain (Contrast) Pituitary was done a year back for irregular periods with raised serum prolactin levels & the finding were consistent with Pituitary Microadenoma measuring 6X6.5 mm in size. Patient underwent Video-EEG monitoring overnight – in which bifrontal & generalized epileptiform discharges were seen. Clinico-electrical data suggested possibility of complex partial seizures with secondary generalization.

Author's Affiliation: *Department of Laboratory Medicine, SAKRA World Hospital, Bangalore.

Reprint Request: Suresh D.R., Associate Consultant, Biochemistry, Department of Laboratory Medicine, Sakra World Hospital, Bangalore, Karnataka-560103.
E-mail: drsuri77@yahoo.com

Serum prolactin levels at 3:41 PM were 5.27 ng/mL on the day of admission & at 4:53 AM on the next day it was 58.37 ng/mL. Early morning sample with high prolactin levels was surprising & there was a clinical disagreement on the Laboratory value. We did a thorough root cause analysis to determine the possibility of any possible pre-analytical, analytical & post-analytical errors for an isolated hyperprolactinemia & find out the etiopathogenesis. Repeat tests on both samples had precise values of 5.31 ng/mL & 58.49 ng/mL. We repeated the serum prolactin test on a fresh sample at 12:25 PM on the same day & the result was 12.48 ng/mL. We also subjected all the three samples for InterLaboratory Comparison with another NABL Accredited Laboratory, Bangalore & the results were within the acceptable precision range.

Discussion

Normal serum prolactin levels vary between 5 and 25 ng/ml in females although physiological and diurnal variations occur. Hyperprolactinemia is considered when fasting levels of serum prolactin are above 25 ng/ml in women at least 2 hours after waking up. It can be symptomatic or asymptomatic. Physiological hyperprolactinemia is usually mild or moderate. Pathological hyperprolactinemia can be caused by both hypothalamic-pituitary disease (prolactinomas) as well as non-hypothalamic-pituitary disease [2,3]. Prolactinomas are divided into: (1) microadenomas (size less than 10 mm) which are more common in premenopausal women, and (2) macroadenomas (size of 10 mm or larger). Women may have menstrual abnormalities, infertility, and decreased bone mass. Hyperprolactinemias can also be due to stress or exercise or by administering antipsychotic or antiepileptic drugs, trauma or chest wall surgery, renal disease, cirrhosis, and seizure within 1-2 hours. These conditions usually cause prolactin elevation of <50 ng/ml. [4]. In this case, patient's MRI Brain was done a year back & was consistent with pituitary microadenoma. But since from one year, patient was asymptomatic, the isolated rise in prolactin at 4:53 AM could not be explained. But patient informed that she had severe discomfort in early morning (when second sample was drawn for prolactin testing), with irregular menstruation episode.

Serum prolactin levels have diurnal variation (higher in the afternoon than in the morning). Unless the prolactin levels are markedly elevated, the investigation should be repeated before labeling the patient as hyperprolactinemic. Even one normal value should be considered as normal and an isolated raised one should be discarded as spurious [5]. In this case, an isolated rise was noticed in 4:53 AM sample & afternoon 12:25 PM sample showed elevated prolactin level compared to previous day's 3:41 PM sample. Studies have suggested a quantitatively greater nocturnal prolactin release around midcycle (eightfold) than during the follicular and the luteal phases (threefold) was found [6]. In this case, the rise was eleven fold & patient was also on neurological medication & thus, a very unique case was reported.

Conclusion

Hence, considering pulsatile secretion and diurnal variation of serum prolactin , an elevated level should always be rechecked before confirming hyperprolactinemia. Blood sample ideally be drawn midmorning and not after stress, venipuncture,breast stimulation, or physical examination, which causes pseudoelevated prolactin levels.

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