

How good is a simple blood test - Prolactin in non-epileptic seizures?

Olivia Watson^{1,2}, Jia (Jenny) Liu^{1,3}, Nevin Kollannoor Chinnan^{1,4,5}

Abstract

Distinguishing epileptic seizures (ES) from non-epileptic seizures (NES) can be difficult, but is important to initiate or modify anticonvulsant treatment. In smaller hospitals where the gold standard of video EEG is unavailable, serum prolactin levels may be used as diagnostic adjuncts. We report a case with significant prolactin elevation but a diagnosis of NES on EEG and seizure semiology, and discuss the limitation of prolactin measurements to distinguish between ES and NES in a postoperative setting.

Keywords: Seizures, Non-Epileptic Seizures, Neurology.

Introduction

An acute postictal serum prolactin rise has been reported as a highly specific indicator of epileptic seizures, but its utility can be affected by the clinical context. We report a case of elevated prolactin in a patient with NES, and discuss the evidence of prolactin as an adjunctive marker for the diagnosis of epilepsy.

Clinical Record

A 30 year old Caucasian female with a background of type 1 diabetes, gastroesophageal reflux and hypertension underwent an uncomplicated intra-operative insertion of an intra-uterine device for menorrhagia management under general anaesthesia. Agents used were propofol 200mg, midazolam 3mg, fentanyl 50micro g and paracetamol 1g. In the immediate postoperative period, she had five brief episodes of tonic clonic seizure-like movements, each lasting a couple of minutes and involving all four limbs and persistent unresponsiveness to deep painful stimuli. She was intubated in the recovery

area using morphine, midazolam and rocuronium, loaded with phenytoin 1 gram and transferred to intensive care. Initial investigations including blood glucose, electrolytes, septic workup, CT brain and transthoracic echocardiogram were unremarkable. Serum prolactin level 20 minutes post-seizure was 3265 mIU/L. Once sedation was turned off, she woke up and responded appropriately to verbal commands and was extubated in an hour. Overnight she had four further episodes of seizure-like activity involving predominantly the upper limbs, each lasting 30seconds to 1 minute. The limb movements were random, asymmetric and asynchronous. She had generalized seizure-like movement once the next morning involving mainly upper limbs, persistent unresponsiveness and an episode of desaturation to SpO₂ 85% after IV midazolam 2 mg. She was then intubated and transferred to a referral hospital for further workup including MRI and EEG. In the referral hospital, she continued to have seizure-like activity and was commenced on a midazolam infusion. MRI brain (including MRV and MRA) with seizure protocol, lumbar puncture and video EEG during seizures were unremarkable. Subsequently, she was weaned off the ventilator and extubated. Repeat observations of the seizure patterns revealed differences compared with her initial

seizures, involving a crying for 'mum' then asymmetric, arrhythmic leg jerks with normal pupillary responses and downgoing Babinski's postictally. As her seizure patterns differed between episodes and were inconsistent with neuroanatomical pathways (bilateral upper limb movements only, asymmetry and arrhythmicity) a diagnosis of NES was made, all anticonvulsants were stopped and she was discharged after three days. Follow-up outpatient EEG and MRI, one month later was unremarkable, there had been no further seizures, and the prolactin levels were in the normal range (310mIU/L).

Discussion

The diagnosis of NES is important for preventing potentially deleterious effects of unnecessary antiepileptic medications, and for early implementation of appropriate psychological treatment [1]. Video EEG is the gold standard for differentiating ES from NES, but is complex, expensive and not available in all settings. An acute postictal serum prolactin rise more than twice the patient's baseline has been reported as a highly specific diagnostic indicator of ES [2] and endorsed as a useful diagnostic adjunct by the American Academy of Neurology to exclude NES [3]. It is thought that ES activity involving the hypothalamus disrupts the suppression of prolactin release by dopamine in the hypothalamus, resulting in an acute prolactin rise [4]. This same mechanism is not said to occur in NES.

¹Department of Intensive Care, Dubbo Base Hospital, Dubbo, Australia.

²School of Rural Health, University of Sydney, Sydney, Australia

³Central Clinical School, University of Sydney, Sydney, Australia

⁴Department of Intensive Care, Taree, NSW, Australia

⁵Conjoint Lecturer, University of Newcastle, NSW, Australia

Address of Correspondence

Dr. Nevin Kollannoor Chinnan
Department of Intensive Care, Dubbo Base Hospital, Dubbo, Australia.
Email: nevinke2001@yahoo.com

© 2017 by Journal of Anaesthesia and Critical Care Case Reports | Available on www.jaccr.com |

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License

(<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Therefore, an acute postictal prolactin rise has been used as a diagnostic biomarker of true ES. Multiple studies have confirmed elevated prolactin as highly specific (89-96%) but poorly sensitive (46-88%) for ES [2,3]. Cragar et al.'s review of 14 studies comparing NES and ES concluded that prolactin elevation after NES is "relatively rare yet may occur" [2]. Mild postictal prolactin rise after NES have been documented, potentially caused by physical activity and stress, but few cases document significant elevation and even these report a significantly greater rise in ES than NES [2,3,5]. Willert et al. conclude that postictal prolactin elevation relative to the patient's baseline is a more reliable marker than absolute prolactin levels, due to large inter- and intra-individual serum prolactin fluctuations [5]. Commonly used criteria for abnormal prolactin are values more than twice the patient's baseline or greater than the upper limit of normal determined by the researchers [4]. In the current case report, the postictal prolactin was indeed compared to the patient's baseline, and shown to be an approximately tenfold elevation. Samples should be collected 10-20 minutes post seizure [3] since prolactin levels decrease with a half-life of 32 minutes [4]. The prolactin level in the current case was taken 20 minutes postictally, and was significantly elevated above normal and above the patient's baseline, noting that it would have been preferable to have a baseline measurement prior to the event. Yet unremarkable investigations and neuroanatomically inconsistent seizure

characteristics led to a diagnosis of NES. Studies of seizure semiology using video EEG diagnoses of ES and NES report an increased likelihood of NES is indicated by features such as a lack of postictal headache or fatigue, and an absence of in-phase upper and lower extremity movements [1]. The patient was not known to have NES prior to the operation, which raised suspicion for ES and influenced the decision to transport to a referral hospital and investigate thoroughly. Other causes of hyperprolactinaemia were ruled out including prolactinoma and drugs including oestrogens, antidepressants, antipsychotics and metoclopramide. Unlike most studies on prolactin in seizures, the initial episode in this case was postoperative. Prolactin rise has been observed postoperatively and post propofol anaesthesia [6,7], furthermore propofol and other anaesthetics have been linked with seizure-like phenomena [8]. Propofol was used in this patient's operation and may be the cause of the prolactin rise, in a case where semiology, unremarkable investigations and lack of recurrence after ceasing antiepileptic drugs led to a NES diagnosis. This report documents a case of significant prolactin rise following NES. This is uncommon and confounding factors including anaesthetic agents or medications may have caused the prolactin rise in the setting of NES. It exemplifies the fact that adjunct tests for distinguishing ES and NES need to be considered in combination and in context. In a smaller hospital where access to neurology specialists, EEG and MRI is limited, alternative methods of

distinguishing between ES and NES are necessary and valuable. Video EEG remains the gold standard but in a resource-limited environment the consideration of adjunct tests can provide useful information, including even mobile phone video footage for examining seizure semiology. This case reminds that caution should be taken when considering serum prolactin especially postoperatively and that these adjunct methods should be considered in combination not alone.

Conclusion

This report documents a case of significant prolactin rise following NES. This is uncommon and confounding factors including anaesthetic agents or medications may have caused the prolactin rise in the setting of NES. It exemplifies the fact that adjunct tests for distinguishing ES and NES need to be considered in combination and in context. In a smaller hospital where access to neurology specialists, EEG and MRI is limited, alternative methods of distinguishing between ES and NES are necessary and valuable. Video EEG remains the gold standard but in a resource-limited environment the consideration of adjunct tests can provide useful information, including even mobile phone video footage for examining seizure semiology. This case reminds that caution should be taken when considering serum prolactin especially postoperatively and that these adjunct methods should be considered in combination not alone.

References

1. Cuthill FM, Espie CA. Sensitivity and specificity of procedures for the differential diagnosis of epileptic and non-epileptic seizures: A systematic review. *Seizure* 2005;14:293-303.
2. Cragar DE, Berry DTR, Fakhoury TA, Cibula JE, Schmitt FA. A review of diagnostic techniques in the differential diagnosis of epileptic and nonepileptic seizures. *Neuropsychol Rev* 2002;12:31-64.
3. Chen D, So YT, Fisher RS. Use of serum prolactin in diagnosing epileptic seizures: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2005;65:668-75.
4. Bauer J. Epilepsy and prolactin in adults: a clinical review. *Epilepsy Res* 1996;24:1-7.
5. Willert C, Spitzer C, Kusserow S, Runge U. Serum neuron-specific enolase, prolactin, and creatine kinase after epileptic and psychogenic non-epileptic seizures. *Acta Neurol Scand* 2004;109:318-323.
6. Celic-Spuzic, E. Effect of anesthesia on the changes in the hormones levels during and after transvesical prostatectomy. *Med Arh* 2011;65(6):348-353.
7. Murakawa T, Tsubo T, Kudo T, Kudo M, Matsuki A. [Effect of propofol as an agent for anesthetic induction on pituitary-adrenocortical function during anesthesia and surgery]. *Masui* 1998;47(11):1350-1357. Japanese.
8. Walder B, Tramèr MR, Seck M. Seizure-like phenomena and propofol: a systematic review. *Neurology* 2002;58:1327-1332.

Conflict of Interest: Nil
Source of Support: None

How to Cite this Article

Watson O, Liu J, Chinnan N K. How good is a simple blood test - Prolactin in non-epileptic seizures? *Journal of Anaesthesia and Critical Care Case Reports* Jan-Apr 2017; 3(1): 20-21.