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Viewpoint

ACTH more than 2000 pg/ml; is it immunoassay interference or another matter?

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INTRODUCTION

Accurate measurement of adrenocorticotropin hormone (ACTH) levels is essential for clinicians to diagnose pituitary and adrenal disorders. We received a serum sample of 55 years gentleman for analysis of morning cortisol and ACTH level. The morning cortisol level was 3.10 µg/dl (3.7-19.4) and ACTH was >2000 pg/ml (7.2-63.4). Primary adrenal insufficiency was suspected based on laboratory data. However, we had barely reported such a higher concentration of ACTH. Several cases of misleading ACTH levels related to heterophilic antibodies have been reported.[1] Immunoassays are vulnerable to occasional analytical errors despite their sensitivity and specificity.

Therefore, careful inspection for potential sources of error in all analytical steps and reanalyzing the serum sample was planned. No preanalytical error was identified in the index case. No issues in the reagent, calibrator, internal quality control graphs, and instrument were identified to label as an analytical errors. The result of repeated serum ACTH was also >2000 pg/ml.

On clinical inquiry, it was found that the patient was a known case of Addison's disease and was recently started with antitubercular therapy after a diagnosis of adrenal tuberculosis. Suddenly his condition was worsened and admitted to the intensive care unit following a diagnosis of Adrenal crisis. Deterioration of his clinical status following antitubercular treatment could be attributed to accelerated cortisol metabolism by induction of cytochrome P450 3A4 by Rifampicin. This led to low cortisol and a very high ACTH level.

Starting rifampicin in patients with Addison's disease or adrenal tuberculosis may precipitate an adrenal crisis as a result of the induction of CYP 3A4 which in turn leads to increased breakdown of cortisol. Therefore, cortisol should be tested in all patients with active tuberculosis infection, especially if there is radiological evidence of adrenal gland involvement. This will help to treat physicians and identify patients at risk of hypoadrenalism prior to starting antitubercular therapy. Nepal harbors numerous cases of tuberculosis. Adrenal insufficiency is a common complication of tuberculosis infection. This letter is written to emphasize the need for caution when prescribing rifampicin for patients with tuberculosis.

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