Austin Journal of Clinical Case Reports

Open Access

Austin Publishing Group

Case Report

Adding on Addison's: A Case Report of Rare Co-Existent Pathology Complicating Acute Pre-Eclampsia (PET) in Pregnancy

Aboda A*, Cahyadi M, Paalendra A, Miller R, Carney T, Aali S and McCully B

Department of Obstetrics & Gynaecology, Mildura Base Public Hospital, Mildura 3500 VIC, Australia

***Corresponding author:** Ayman Aboda, Department of Obstetrics & Gynaecology, Mildura Base Public Hospital, Mildura 3500 VIC, Australia

Received: April 08, 2022; **Accepted:** April 29, 2022; **Published:** May 06, 2022

Abstract

Addison's disease is a rare condition, which world-wide, may affect many millions of people. In pregnancy however, it has been rarely reported and, in this setting, remains poorly understood. What we do know, is that it is an endocrine disorder characterized by adrenal insufficiency leading to decreased production of cortical hormones including most notably, cortisol, but also the androgens and aldosterone. The sequaelae may be varied but most significantly, can lead to a loss of the body's normal resilience to stress and injury.

We present the case of a 35-year-old woman who presented in late pregnancy with signs and symptoms of fulminating pre-eclampsia (PET). Paradoxically, she was found to have electrolyte abnormalities which persisted despite appropriate treatment. These were suggestive of an underlying endocrine disorder and she was subsequently diagnosed with atypical Addison's disease. With appropriate management, she was stabilized and delivered safely.

We report this as a rare example of newly diagnosed Addison's disease discovered for the first time in late pregnancy. It highlights that although rarely diagnosed, early identification can help avoid potentially life-threatening sequalae such as acute adrenal insufficiency as well as complications including preterm birth, neonatal hypoglycaemia and prolonged hospital admission. This calls for ongoing vigilance in clinical care, and the continuous improvement of shared knowledge through collaborative communication and awareness of evidence based, best practice guidelines.

Keywords: Addison's disease; Pre-eclampsia; Collaborative

Background

Addison's disease or acquired primary adrenal insufficiency is a condition where adrenal hormones such as the glucocorticoids and mineralocorticoids are below normal levels. It is a relatively rare condition, with incidence ranging around 1 per 10,000 people. Untreated, symptoms are generally nonspecific and benign. They may include fatigue, nausea, vomiting, loss of weight, salt cravings, musculoskeletal pain, and postural dizziness or hypotension, many of which may reflect autoimmune or vascular changes as well as metabolic and electrolyte imbalance [1]. Of note, many of these symptoms along with other cardinal features such as increased pigmentation, are also found in pregnancy. More significantly however, the disease if untreated, may compromise the ability to respond appropriately to stress and injury which may lead to life threatening cardiovascular collapse - an Addisonian Crisis. We note that pregnancy is a state of many potential stressors. These may occur as part of normal adaptation during the physiological journey of birth or, as described in this case report, a promulgation of risk associated with complications such as pre-eclampsia and inadvertently, the challenge of iatrogenic intervention, including emergency delivery.

Newly diagnosed Addison's disease in pregnancy, has been rarely documented, hence its effects are largely unknown. In this case report, it was discovered fortuitously in the setting of unexplained hypokalaemia which had responded poorly to replacement therapy. This is unusual, as most cases of Addison's disease are associated with high potassium levels - we propose that this was either a rare variance of normal or more probably, a result of altered renal function consequent to PET. More commonly, Addison's disease in pregnancy will present as a previously known condition. In this setting, we are more fortunate as there is opportunity to safeguard against sequalae such as the risk of Addisonian crisis which could be devastating in the gravid patient where both mother and baby are vulnerable to harm [2].

Treatment of Addison's disease requires replacement of adrenal hormones, most notably, the glucocorticoids but may also include the mineralocorticoids. In our patient, Hydrocortisone (Cortisol) was given prior to the onset of delivery and thereafter, in 2 divided daily doses, to simulate normal secretory circadian rhythms. Adequacy of treatment was gauged by normalization of electrolytes, most notably potassium and sodium, and normal plasma renin concentrations [3].

Case Presentation

A 35-year old, multigravida patient at 36+1 weeks, presented acutely to our Maternity Assessment Unit (MAU), with bowel and joint pain, lethargy, and low appetite on a background of known

Citation: Aboda A, Cahyadi M, Paalendra A, Miller R, Carney T, Aali S, et al. Adding on Addison's: A Case Report of Rare Co-Existent Pathology Complicating Acute Pre-Eclampsia (PET) in Pregnancy. Austin J Clin Case Rep. 2022; 9(3): 1249.

mild pre- eclampsia which up until that time, had been managed expectantly in community. She had a BMI of 39.9 and had one prior antenatal visit recorded at 34 weeks. Prior to this, she had received care in family practice with records indicating normal first trimester blood screening and morphology at 20 weeks, as well as a normal glucose tolerance at 28 weeks. At the time of her visit, she had mild, isolated hypertension that was managed conservatively with low dose Labetalol. She also had mild iron deficiency anaemia treated with oral supplementation. Her past history included two normal births with a previous partner and more recently, an emergency Caesarean section at 36 weeks for failed induction of labour following pre-term, spontaneous rupture of membranes. She had had one spontaneous miscarriage at 5 weeks shortly before her current pregnancy which was managed expectantly. There were no other antecedent medical or surgical concerns.

On arrival to MAU, her BP was 150/90 and ward test urine positive for protein. Her urine protein creatinine ratio was elevated at 41.77 mg/mmol (<30). Her blood workup demonstrated elevation of liver transaminases and serum urate indicative of evolving PET. She was admitted for observation and stabilization using an increased dose of Labetalol with the addition of oral hydralazine. Her blood pressure remained labile and though her symptoms appeared well tolerated, a decision for early birth at 37 weeks was thought to be best management. Given her previous history of operative delivery, an elective Caesarean section was decided upon.

Up to the time of delivery, she was noted to have hypokalaemia 2.9mmol/L (normal levels between 3.6 and 5.2 mmol/L) which paradoxically, remained resistant to intravenous replacement therapy with levels rising at most, to only 3.2mmol/L. In consultation with medical colleagues, a serum cortisol was arranged and found to be reduced at 48nmol/L (normal 185-624). This suggested an underlying endocrine dysfunction. She had however, been given intramuscular betamethasone in the days just prior to the test. This is a steroid injection given to protect newborns against the risk of respiratory distress when delivery is expected prior to term. Although this may have caused some degree of iatrogenic cortisol suppression, the possibility of an Atypical Addisonian comorbidity was still considered and the patient was given intravenous hydrocortisone on the morning of surgery to mitigate the risk of crisis. She had an uncomplicated procedure and gave birth of a healthy baby weighing 3160g.

In the days following, her symptoms of PET abated. A repeat serum cortisol was again reduced at 102nmol/L. ACTH levels were 13.4ng/L (7.2-63.3 ng/L) and a short Synacthen test positive with baseline cortisol level of 73nmol/L, rising to 270nmol/L at 30 minutes and 382nmol/L at 60 minutes, both less than the expected rise of >460nmol/L. A diagnosis of primary adrenal insufficiency was confirmed. Additional testing included normal CT scan of abdomen and negative assay for adrenal antibodies. Aldosterone-renin ratio (ARR) was normal on two occasions, 20 and 10 respectively (<70). Hydrocortisone was prescribed (20mg mane, 10mg each afternoon) and cortisol level rose appropriately to 126nmol/L with continued treatment. She was discharged 4 days after delivery, her BP had returned to normal and her magnesium and potassium levels also returned to normal.

Discussion

The case presents a woman in late pregnancy with PET. PET is a relatively common complication of pregnancy, occurring in approximately 10% of cases. It is frequently associated with underlying maternal vascular or endocrine dysfunction such as diabetes or essential hypertension, but has rarely been cited in association with newly diagnosed Addison's disease. The diagnosis was unexpected, prompted by investigation of an unexpected and persistent hypokalaemia. This is not typically a hallmark of Addison's disease, where, more commonly, raised serum levels are expected [4]. The case thus presents a finding rarely documented in other reports [5]. We speculate that this may have occurred secondary to renal dysfunction promulgated by PET leading to excessive urinary loss and thus overriding the tendency of Addison's to raise serum levels [8,9].

Similarly, and with equal rarity, hypomagnesaemia, was a persistent finding in our case. This is unusual in Addison's Disease, and is found in only 5% of cases [6,7] and we suggest, may reflect a confounding electrolyte disturbance created by PET. It is significant because magnesium in the form of sulphate, is an important treatment for the cerebral irritability of PET. Low levels may thus contribute to the symptomatology of clinical presentation [9,10].

Hypertension is commonly seen in patients with Addison's disease. Approximately 20% of patients will have a history of essential hypertension. This is significant as it may create a background risk of vascular disease and thus the development of hypertensive disorders in pregnancy, including PET.

A diagnosis of Addison's disease is unusual and difficult to make as clinically will be apparent after damage of about 80-90% of adrenal cortices [11-13]. It's call signs may be subtle. This is particularly so when a patient presents in pregnancy with the relatively common and overarching findings of acute PET. In this setting, signs and symptoms are all too readily attributed to the most likely cause, and further thought of other morbidity rarely considered. In our case, confirmation of Addison's disease was providential, elucidated only by a suspicion of underlying endocrine disorder based on continued abnormalities of electrolyte balance. The findings themselves were not characteristic of known pathology, it was moreover the persistence of change that led to enquiry rather than the change itself. We acknowledge the diligence of our colleagues for the perspicacity of their efforts. It was an important undertaking, because left undiscovered, Addison's disease can make primary care more difficult, or more subtly, undermine the efficacy of established treatment regimens. More significantly, it may agitate an acute crisis, such as may follow the morbidity of a known pregnancy complication such as PET, or, as may more often be the case, the additional burden of medical intervention such as induced delivery or emergency surgery. In the long term, Addison's disease may affect future pregnancies, with reports suggesting an increase in adverse outcomes, possibly related to a lack of maternal glucocorticoids creating a state of foetal stress, thereby increasing foetal glucocorticoid and placental CRH production, which may predispose to preterm delivery [14,15]. For patients with known disease, additional care during subsequent pregnancy is needed as many of the symptoms traditionally used to monitor the adequacy of treatment, are commonly seen as part of

normal pregnancy transition, such as nausea, tiredness, weight gain, and striae, thus leading to potential miscalculation of dosage regimes [2].

Conclusion

Addison's disease is a rare condition that may often only be suspected by the presence of electrolyte imbalance. Its symptoms are generally vague and may easily be overlooked in the absence of diligent search. More distressingly, it may present as an acute crisis, where circulatory and haemodynamic collapse badgers the response to stress or injury. Our case report presents the finding of atypical Addison's disease in late pregnancy. We cannot say for sure whether it was pre-existent and thus perhaps in some way contributed to the aetiology of PET, or, whether it arose as an event itself of the vascular pathophysiology of PET leading to adrenal cortical injury, though admittedly, this would be very unlikely.

By making a diagnosis, we were able to avert the possibility of Addisonian crisis that may have followed emergency surgery, or indeed, the cumulative stresses of coping with PET and the ordeals of post- partum recovery. We were able to ensure best possible recovery with the normalization of endocrine function which as noted, may promote optimal wellbeing not only for future life and pregnancies, but also for immediate motherhood and breastfeeding.

This case report highlights Addison's disease in continued medical education. It demonstrates the importance of vigilance, and of networking when required, within a broad, multidisciplinary team environment to encourage shared decision making and collaboration of clinical experience to provide best possible patient care. By sharing these experiences, we help expand clinical guidelines and through knowledge, individual expertise.

References

1. Burton C, Cottrell E, Edwards J. Addison's disease: identification and management in primary care. Br J Gen Pract. 2015; 65: 488-490.
2. Oliveira D, Lages A, Paiva S, Carrilho F. Treatment of Addison's disease during pregnancy. Endocrinol Diabetes Metab Case Rep. 2018; 2018.
3. Bandoli G, Palmsten K, Forbess Smith CJ, Chambers CD. A Review of Systemic Corticosteroid Use in Pregnancy and the Risk of Select Pregnancy and Birth Outcomes. Rheum Dis Clin North Am. 2017; 43: 489-502.
4. Saevik AB, Akerman AK, Gronning K, Nermoen I, Valland SF, Finnes TE, et al. Clues for early detection of autoimmune Addison's disease - myths and realities. J Intern Med. 2018; 283: 190-199.
5. Abdalla M, Dave JA, Ross IL. Addison's disease associated with hypokalemia: a case report. J Med Case Rep. 2021; 15: 131.
6. Inder WJ, Meyer C, Hunt PJ. Management of hypertension and heart failure in patients with Addison's disease. Clin Endocrinol (Oxf). 2015; 82: 789-792.
7. Erbas IM, Altincik SA, Catli G, Unuvar T, Ozhan B, Abaci A, et al. Does fludrocortisone treatment cause hypomagnesemia in children with primary adrenal insufficiency? Turk J Med Sci. 2021; 51: 231-237.
8. Lin SH, Lin YF, Chen DT, Chu P, Hsu CW, Halperin ML. Laboratory tests to determine the cause of hypokalemia and paralysis. Arch Intern Med. 2004; 164: 1561-1566.
9. Anthony O, Peter E, Onyeka N, Aloysius O, Virginus M. Determination of Serum Electrolyte Levels in Pregnant Women Observed With Preeclampsia during Pregnancy. JMSCR. 2015; 3: 3830-3836.
10. Enaruna NO, Ande A, Okpere EE. Clinical significance of low serum magnesium in pregnant women attending the University of Benin Teaching Hospital. Niger J Clin Pract. 2013; 16: 448-453.
11. Alevritis EM, Sarubbi FA, Jordan RM, Peiris AN. Infectious causes of adrenal insufficiency. South Med J. 2003; 96: 888-890.
12. Dawoodji A, Chen JL, Shepherd D, et al. High frequency of cytolytic 21-hydroxylase-specific CD8þ T cells in autoimmune Addison's disease patients. J Immunol. 2014; 193: 2118-2126.
13. Hellesen A, Bratland E. The potential role for infections in the pathogenesis of autoimmune Addison's disease. Clin Exp Immunol. 2019; 195: 52-63.
14. Hopper J Jr, O'Connell BP, Fluss HR. Serum potassium patterns in anuria and oliguria. Ann Intern Med. 1953; 38: 935-954.
15. Bjornsdottir S, Cnattingius S, Brandt L, Nordenstrom A, Ekbom A, Kampe O, et al. Addison's disease in women is a risk factor for an adverse pregnancy outcome. J Clin Endocrinol Metab. 2010; 95: 5249-5257.