Case Report

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What is the materno-fetal prognosis of adrenal insufficiency and pregnancy in low-resource setting? a case report

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Introduction and importance: Adrenal insufficiency is a rare chronic disease with a prevalence of 39 to 60 cases per million peoples in Europe. However, the prevalence is higher in sub-saharian Africa. The occurrence of pregnancy in adrenal insufficiency is rare but associated with high maternal and perinatal morbidity and mortality. For this reason, the management of pregnancy in adrenal insufficiency patient must be provided by a multidisciplinary team.

Case presentation: The authors report the case of a 34-year-old pregnant woman followed for adrenal insufficiency secondary to prolonged corticosteroid therapy. Treatment consisted to an obstetrical and endocrinological follow-up and corticosteroid replacement therapy with hydrocortisone. A prophylactic cesarean section at 38 weeks resulted in the birth of a newborn male weighing 3395 g. Maternal and perinatal prognosis was good.

Clinical discussion: Pregnancy in adrenal insufficiency is a therepeutic challenge in developing countries. Through this case, the authors discuss the therapeutic and prognostic aspects of adrenal insufficiency in our setting.

Conclusion: With the introduction of gluco-corticosteroid replacement therapy, pregnancy in adrenal insufficiency can progress normally.

Keywords: adrenal insufficiency, corticotherapy, corticotropic insufficiency, pregnancy

Introduction

Adrenal insufficiency includes all conditions in where the secretion of adrenocortical hormones, mainly glucocorticoids and/or mineralocorticoids, falls below the body's needs. A distinction is made between primary insufficiencies or Addison's disease and secondary insufficiencies, or corticotropes insufficiencies, by pituitary or hypothalamic damage[1,2]. Secondary adrenal insufficiency is due to morphogenesis abnormalities, hypothalamic or pituitary organic damage and prolonged corticosteroid therapy[3]. It is a rare and unusual chronic disease in pregnant women with an incidence of 5.6 to 9.6 per 100 000 pregnancies[4]. It makes pregnancy a high-risk pregnancy with high maternal and perinatal morbidity and mortality (occurrence of potentially fatal acute adrenal insufficiency in 69%, post-partum hemorrhage, thromboembolic accident, early abortion,

HIGHLIGHTS

- Adrenal insufficiency is a rare and unusual chronic disease in pregnant women with high maternal and perinatal morbidity and mortality.
- Management by glucocorticosteroid therapy should take into account the physiological changes of the corticotropic axis during pregnancy as well as the side effects of glucocorticoids on the evolution of pregnancy.
- A 34-year-old women, gravida 5, para 3, mother of three living children who was diagnosed with adrenal insufficiency 3 years ago was admitted to our department for management of a 28 week pregnancy on the ground of adrenal insufficiency.
- Treatment consisted to an obstetrical and endocrinological follow-up and corticosteroid replacement therapy with hydrocortisone that occurring in good maternal and perinatal prognosis.
- The authors discuss the therapeutic and prognostic aspects of adrenal insufficiency and pregnancy through this case report and a literature review.

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grow restriction, death in utero, low birth weight, neonatal death)[4]. Management by glucocorticosteroid therapy should take into account the physiological changes of the corticotropic axis during pregnancy as well as the side effects of glucocorticoids on the evolution of pregnancy. Adrenal insufficiency in pregnancy is life-threatening in developing counties. We report a case of adrenal insufficiency and pregnancy in a 34-year-old patient. We discuss the therapeutic and prognostic aspects of this rare condition through this observation and a literature review. This case recalls the difficulties of management of adrenal insufficiency during pregnancy in a low-resource country and show a management guideline for practitioners in a low-resource setting. This work has been reported in line with the Surgical CAse REport (SCARE) 2023 Criteria[5].

Case presentation

It was a 34-year-old black African women, gravida 5, para 3, mother of three living children. She was diagnosed with adrenal insufficiency 3 years ago and well monitored with hydrocortisone 20 mg in the morning and 10 mg in the evening. In her medical history, there was a herniated disc treated by corticoid injections and prolonged oral corticosteroid therapy for 1 year. She was admitted to our department for management of a 28 week pregnancy on the ground of adrenal insufficiency. The general examination revealed a good general condition. The conjunctivae and mucous membranes as well as the integuments were normally colored, arterial pressure at 110/80 mmHg, temperature at 36.2°, respiratory rate at 14 mvts/mn, heart rate at 87 btm/mn. Weight at 117 kg with a BMI at 38.3 Kg/m^2. On obstetrical examination we noted a fundal height of 28 cm. On vaginal examination, the cervix was short posterior and dehiscent. The obstetrical ultrasound showed an evolving single-fetal pregnancy of 28 weeks with no anomaly of the fetus and the annexes. The biological assessment noted a hemoglobin level at 11.8 g/dl, blood sugar at 0.69 g/l. Electrolyte ionogram, renal and hepatic assessments were unremarkable. The 8 h cortisol level was at 70.2 nmol/l (normal values: 260–720 nmol/l), the TSH was normal at 2.05 mIU/l, the adrenocorticotrophic hormone had collapsed with a rate of 6.84 pg/ml. Throughout the pregnancy, a multidisciplinary follow-up (obstetrician-gynecologist, endocrinologist, internist, and resuscitator anesthesiologist) was established. The dose of hydrocortisone was adapted to 100 mg/12 h per os. The Figure 1 presents cortisol and adrenocorticotrophic hormone values before pregnancy, during pregnancy, and in the postpartum period. The patient was reviewed in prenatal consultation every 2 weeks until 38 weeks of pregnancy when a prophylactic cesarean section was performed. The cesarean was uneventful under general anesthesia with the birth of a newborn male weighing 3395 g, Apgar at 8–10. The established medical management protocol was as follows: administration of 100 mg of hydrocortisone in infusion at induction, postoperatively we administered 100 mg of hydrocortisone in infusion every 12 h for 48 h and then a reduction in dose at 50 mg/12 h, then passage to the oral route at the usual doses before pregnancy. The postpartum period was without maternal or neonatal complications. The patient was discharge in good clinical and biological condition. Three months later the patient had presented no complications. The patient is satisfied with the treatment. The patient is currently being followed by an endocrinologist team.

Discussion

This observation reports the therapeutic and prognostic aspects of a case of pregnancy in adrenal insufficiency complicating prolonged corticosteroid therapy poorly conducted in a low resources center. The occurrence of pregnancy in patient with adrenal insufficiency is an exceptional condition. Adrenal insufficiency is a rare chronic disease with a prevalence of 39–60 cases per million peoples in Europe[3]. In Africa, a Tunisian retrospective study over 17 years found 92 cases of adrenal insufficiency[6]. The prevalence is higher in black Africa. Indeed, in Niger, a prospective study over one year found 31 cases of adrenal insufficiency[2]. It particularly affects women with a sex ratio Man/Female of 0.069[2]. This female predominance in sub-Saharan Africa is caused by the voluntary depigmentation with topical corticosteroids that cause secondary adrenal insufficiency, which is more common in women in our regions[2,7]. In this case, adrenal insufficiency is the result of prolonged oral corticosteroid therapy in a context of herniated spinal disc. Etiologically, the etiologies of primary adrenal insufficiency are: congenital adrenal hypoplasia, adrenoleukodystrophy (ALD), resistance to adrenocorticotrophic hormone (ACTH) syndrome, autoimmune causes (approximately 70% of cases observed in industrialized countries), infectious causes (HIV and Tuberculosis), vascular causes, adrenal metastases, and iatrogenic causes. Secondary adrenal insufficiency is due to morphogenesis abnormalities, hypothalamic or pituitary organic damage and prolonged corticosteroid therapy[2,3] as in our case. During pregnancy it causes a real therapeutic problem. The objective of monitoring during pregnancy is to maintain glucocorticosteroid replacement therapy at doses ensuring good maternal and fetal status while avoiding underdosing (causing the occurrence of potentially fatal acute adrenal insufficiency, low weight birth, and a maternal electrolyte disorder) or an overdose (causing gestational diabetes, macrosomia, and hypertension or even pre-eclampsia)[8]. Regarding gluco-corticosteroid replacement therapy during pregnancy, the ideal regimen is poorly defined but dose adjustment according to gestational age is recommended[8,9]. A 20–40% increase is usually needed after the 24th week to mimic the physiological elevation of cortisol levels at this time of a normal pregnancy[8,9]. Hydrocortisone does not cross the placental barrier because it is effectively inactivated in the placenta[8–10]. Therefore, hydrocortisone is the treatment of choice for corticosteroid replacement therapy during pregnancy. The daily doses used generally vary between 20 and 25 mg of hydrocortisone divided into two or three daily intakes, with 50 to 75% of the daily dose administered in the early morning to mimic the physiological pattern of cortisol secretion[10]. Monitoring of glucocorticoid therapy is based on clinical signs as no objective assessment based on laboratory examinations has been proven reliable[9,10]. However, fairly unspecific signs of overdose (stretch marks and weight gain) or underdose (tiredness, nausea, and vomiting) of glucocorticoids are frequently present in pregnant women. Therefore, therapeutic education is essential with regard to self-adjustment of hydrocortisone doses or self-injection of hydrocortisone in the event of illness or vomiting. The patient must carry an adrenal insufficiency card and be able to recognize clinical situations requiring hospital treatment[8]. Regarding mineralocorticoid supplementation in primary adrenal insufficiency, fludrocortisone is mainly used as a mineralocorticoid substitute in Addison's disease. In fact, mineralocorticoid requirements may increase

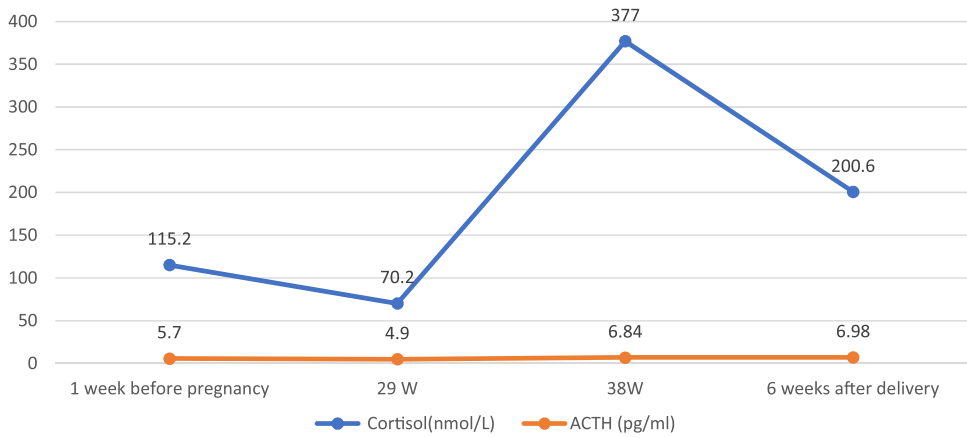

Figure 1. Cortisol and adrenocorticotrophic hormone values before pregnancy, during pregnancy, and in the postpartum period.

slightly in the last trimester due to the antimineralocorticoid effects of progesterone. Clinical parameters such as signs of orthostatic hypotension and increased serum potassium should govern dose adjustment. Similarly, fludrocortisone should be reduced in case of hypertension and/or hypokalaemia and even withdrawn in case of pre-eclampsia. In contrast, plasma renin cannot be used as a reliable marker to adjust mineralocorticoid dosage during pregnancy[9]. Childbirth is a high-risk period for acute adrenal insufficiency. Childbirth must therefore be planned and managed by a multidisciplinary team. Most births proceed without complications when the pregnancy has been carefully monitored and the treatment optimized. The endocrinologist should provide the obstetrical team with a written treatment protocol regarding intravenous glucocorticoid coverage, which should be started before the active phase of labor. The most commonly used protocol consists of: an initial bolus of 100 mg of hydrocortisone followed by a continuous infusion of 200–300 mg/24 h[8,10]. In postpartum period, twice the dose of hydrocortisone used during gestation can be resumed after delivery for 24–48 h. After that, if the patient is clinically in good condition, she can be quickly reduced to the usual doses used before pregnancy[8]. Concerning prognosis: according to data from recent literature, no case of maternal death related to adrenal insufficiency has been reported[9]. Several authors have reported cases of acute adrenal insufficiency successfully treated[11,12]. However, various obstetric complications have been described. Grow restriction was reported in 4.2% of pregnancies[9]. In the study by Kubler *et al.*[13] of 31 pregnancies in 21 patients with hypopituitarism, the rate of low weight for gestational age was 38% compared to 12.7% in the control group. The authors explain its results by placental insufficiency in these patients. In the same study, cesarean delivery was very high (89 vs 11.4%) as was postpartum hemorrhage (5.26% vs 1%). The high cesarean section rate was partly due to more obstructed labor presentations and partly due to the recommendation of the obstetrical team[9] as was the case in this observation. Gradden *et al.*[14] reported a case of abortion at 11 weeks in an unrecognized Addisonian whose diagnosis was made in the context of persistent gravidic vomiting. Otta *et al.*[14,15] reported a case of neonatal death, 8 h after delivery in an Addisonian who was noncompliant for her glucocorticoid treatment during pregnancy. In this case, no maternal or perinatal complications were observed.

Conclusion

As this case demonstrates, pregnancy is possible in case of adrenal insufficiency and can evolve normally with good multidisciplinary care. Hormone replacement therapy based on hydrocortisone makes it possible to observe a favorable evolution. The occurrence of acute adrenal insufficiency should be an obsession and therapeutic education is an essential part of care. Patients should always carry an Addisonian card.

Ethical approval

The publication of this case report has been authorized by the quality service of our institution because case reports are exempted from ethical approval in our institute (Abdou Moumouni University, National hospital of Niamey, Niger).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

H.S.D., and O.Z.A.: were involved in study conception and design, and participation in patient treatment, surgery, data collection, manuscript drafting, draft review, and manuscript finalization; M.C.Y., M.O., S.G., A.A., M.S.M.A., and M.N.: participated in patient treatment, data collection, data analysis and interpretation, and draft manuscript review for intellectual content. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

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Data availability statement

Supplementary data to this article can be found from the corresponding author.

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References

[1] Mosnier-Pudar H. Adrenal insufficiency. Encycl Med Chir Elsevier, Paris 1998;3:4.
[2] Mahamane Sani Ma, Apetogbo Kd, Maazou ML, *et al*. Etiologies of adrenal insufficiency in Niger. J Rech Science Univ Lomé (Togo), Special 2019;21:327–34.
[3] Gatta B, Monsaigeon M, Tabarin A. Adrenal insufficiency. Medical-Surgical Encyclopedia. Nutrition Endocrinol 2003;10-015-A- 10:15.
[4] Gardella B, Gritti A, Scatigno AL, *et al*. Adrenal crisis during pregnancy : case report and obstetric perspective. Front Med 2022;9:891101.
[5] Sohrabi C, Mathew G, Maria N, *et al*. The SCARE 2023 guideline: updating consensus Surgical CAse REport (SCARE) guidelines. Int J Surg Lond Engl 2023;109:1136–40.
[6] Makni S, Ben Messaoud I, Akad T, *et al*. Adrenal insufficiency : Tunisian retrospective study about 92 cases. Archives de pédiatrie 2010;17:96.
[7] Ajose FO. Consequences of skin bleaching in Nigerian men and women. Int J Dermatol 2005;44:41–3.
[8] Oliveira D, Lages A, Paiva S, *et al*. Treatment of Addison's disease during pregnancy. Endocrinol Diab Metabol 2018;2018:17–0179.
[9] Anand G, Beuschlein F. Management of endocrine disease : fertility, pregnancy and lactation in women with adrenal insufficiency. Eur J Endocrinol 2018;178:R45–53.
[10] Lebbe M, Arlt W. What is the best diagnostic and therapeutic management strategy for an addison patient during pregnancy ? Clin Endocrinol 2013;78:497–502.
[11] Seaward PG, Guidozzi F, Sonnendecker EW. Addisonian crisis in pregnancy. Case report. Br J Obstet Gynaecol 1989;96:1348–50.
[12] Aboda A, Cahyadi M, Paalendra A, *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;9:1249.
[13] Kubler K, Klingmuller D, Gembruch U, *et al*. High-risk pregnancy managment in women with hypopituitarism. J Perinatol 2009;29:89–95.
[14] Gradden C, Lawrence D, Doyle PM, *et al*. Addison's disease in pregnancy. Lancet 2001;357:1197–.
[15] Fux Otta C, Szafryk de Mereshian P, Iraci GS, *et al*. Pregnancies associated with primary adrenal insufficiency. Fertil Steril 2008;90:e1117–20.