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Diabetes Insipidus and Pregnancy: A Case Report from Casablanca University Hospital (IBN ROCHD Maternity Hospital)

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Abstract

Diabetes insipidus (DI) is a rare condition that complicates around two to three pregnancies out of 100,000 **[1]**. It is generally revealed by a polyuro-polydipsic syndrome or by serious hydro-electrolytic decompensations, mainly with neurological symptoms. The aetiologies of diabetes insipidus during pregnancy are either specific to pregnancy or gestational diabetes insipidus, or discovered before pregnancy. Gestational DI can occur in the absence of any obstetric pathology, in which case its pathophysiology can be explained by interactions between the placenta and ADH metabolism. Although there is no clear evidence of a direct link between gestational diabetes and pre-eclampsia, the frequent association observed between these two conditions may be explained by their occurrence in a high-risk environment. However, the polyuro-polydipsic syndrome is a symptom that is often trivialised by patients and may be reported spontaneously, so its frequent association with serious obstetric pathologies justifies its systematic investigation by questioning.

Keywords: Diabetes Insipidus; Pregnancy; Polyuro Polydipsic Syndrome

Abbreviations: DI: Diabetes Insipidus, ADH: Antidiuretic Hormone, HCG: Chorionic Gonadotrophic Hormone

Introduction

Diabetes insipidus (DI) is a rare condition that complicates around two to three pregnancies out of 100,000 **[1]**. It is generally revealed by a polyuro-polydipsic syndrome or by serious hydro-electrolytic decompensations, mainly with neurological symptoms. The aetiologies of diabetes insipidus during pregnancy are either specific to pregnancy or gestational diabetes insipidus, or discovered before pregnancy. The pathophysiological mechanisms underlying the appearance of a polyuro-polydipsic syndrome during pregnancy are closely linked to interactions between the hypothalamic-pituitary axis, the placenta and the maternal liver, with the predominant mechanism varying according to the aetiology.

Patient and Observation

Mrs K.M aged 36, III G IIIP (3 EV / CZR), T2DM for 2 years on insulin, was admitted to hospital at 34 weeks' amenorrhoea (SA) for glycaemic imbalance complicated by macrosomia

and hydramnios. The patient was referred to emergency by her endocrinologist for strict glycaemic monitoring. After an aetiological and morphological assessment of the hydramnios and macrosomia and a complete degenerative diabetes work-up, which proved to be normal, the patient presented with a polyuro-polydipsic syndrome associated with intense headaches during her hospitalisation. Her daily water intake was approximately 10 litres per day at the time of her hospitalisation. No digestive symptoms or signs of dehydration were observed, and the neurological examination was normal. The clinical examination showed no signs of associated pre-eclampsia.

Glycaemic monitoring showed high values without glycosuria. Glycaemic control was obtained after modification of insulin doses and a strict diet.

Biological tests showed normal plasma osmolality and natraemia, and normal renal function tests. Urines taken over 24 hours showed a low urine specific gravity of 900 and a urine osmolality of 91 mosm/kg with no proteinuria; MRI did not reveal any process in the hypothalamo-hypophyseal region. Given this isolated polyuro-polydipsic syndrome, the diagnosis of gestational diabetes insipidus was made, treatment with Minirin was instituted and daily clinical and biweekly biological monitoring was carried out. Clinically, the polyuro-polydipsic syndrome remained stable, with an input/output balance varying between 5 and 6 L/d. Caesarean section was indicated at 38 + 6 days' gestation, and spinal anaesthesia was performed with increased crystalloid filling, resulting in the delivery of a baby weighing 3700 g with an Apgar score of 10/10. At the end of the operation, postoperative diuresis was 600 ml.

The evolution was marked by the appearance in the immediate postoperative period of motor and sensory deficits in all 4 limbs. A radiological and biological work-up was carried out, which returned to normal, and the patient was transferred to intensive care. Postpartum fluid intake decreased to 3 litres per day on day 6. Given the good progress, the patient was discharged at 10 days postpartum and a consultation was scheduled.

Discussion

Gestational diabetes insipidus can complicate one pregnancy in 30,000, its incidence is 100 times rarer than the polyuro-polydipsic syndrome that can occur during SHAG. Pre-gestational diabetes is a major risk factor for the occurrence of isolated diabetes insipidus. The polyuro-polydipsic syndrome, found in diabetes insipidus, is defined by an increase in 24-hour urine volume of up to 15 litres per day. It is associated with a sensation of thirst and may be complicated by major electrolyte disorders such as dehydration. Antidiuretic hormone (ADH) plays a key role in the pathophysiology of ID. It is synthesised by the supraoptic nuclei of the hypothalamus and released by the posthypophysis, acting on the collecting ducts by increasing water permeability. During pregnancy, a fall in natremia and plasma hypoosmolalite can be observed from the sixth week **[2]**. However, following a simultaneous lowering of the thresholds for ADH release and thirst, polyuria does not occur and ADH synthesis remains constant. This mechanism, which is specific to pregnancy, is probably due to the action of chorionic gonadotrophic hormone (HCG) **[3]**. ADH metabolism is also altered during pregnancy due to the presence of a placental vasopressinase. This aminopeptidase, secreted by trophoblastic cells, inactivates vasopressin and oxytocin **[4]**. A correlation has been shown between circulating levels of this placental vasopressinase and clearance of endogenous ADH **[4,5]**. Concentrations of this enzyme increase during the last two trimesters and are proportional to placental mass **[6]**. There are therefore specific causes of DI during pregnancy due to an excess of vasopressinase. In some cases, this may be due to an increase in its half-life as a result of reduced hepatic metabolism: this is the case with the hepatic dysfunctions found in SHAG **[7]** or HELLP syndrome **[8,9]**. In other cases, the mechanism involved is simply an excess of vasopressinase production due to increased placental mass, leading to increased catabolism of ADH: in this case, as in our clinical case, we speak of gestational DI.

DI may pre-exist pregnancy: central DI sensitive to ADH or nephrogenic DI, insensitive to ADH **[10]**. The link between pre-eclampsia without liver damage and ID is more controversial. Some have attributed this association to a direct hypertensive property of the C-terminus of the degradation product of vasopressin by vasopressinase **[11,12]**. However,

it would appear that this explanation is not sufficient, as no increase in the activity of the specific receptor has been demonstrated **[13,14]**. The pathophysiology of the polyuro-polydipsic syndrome during pregnancy therefore justifies looking for an increase in urine volume in pre-eclampsia, which may mark the onset of an ID, and also closely monitoring the development of gestational ID to check whether it remains isolated. When a polyuro-polydipsic syndrome is discovered during pregnancy, measurement of daily diuresis and urinary and plasma osmolalite will confirm the diagnosis of ID. The initial work-up will help to differentiate between the various aetiologies. DI associated with true obstetric emergencies of the HELLP or SHAG type, requiring appropriate management, will be distinguished from isolated gestational DI. A biological work-up including a proteinuria test, platelet count, haemostasis test, complete liver work-up and blood ionogram with urea and creatinine will enable us to check for the association with a pathology specific to pregnancy (pre-eclampsia, HELLP-syndrome, SHAG, etc.) requiring urgent treatment. An assessment of the impact on the foetus (ultrasound, monitoring) and the mother (renal assessment, weight). An MRI of the sella turcica will be used to complete the aetiological work-up and rule out a tumour cause. Measurement of urinary and plasma ADH is useless and costly in this context. The diagnosis will be confirmed at a distance by measuring urinary osmolality before and after a water restriction test, which is the main diagnostic test outside pregnancy. This test can be dangerous and is not recommended during pregnancy. The main test for confirming the diagnosis during pregnancy is a therapeutic d'DAVP administration test, combined with measurement of urinary osmolality. The specific management of gestational DI is mainly based on the administration of Minirin1 or d'DAVP or 1-deamino-8-AVP, a vasopressin analogue. This is a vasopressin analogue with a terminal end not degradable by vasopressinase. The most commonly used route is the intra-nasal route. There is no recommended optimal dose, but by gradually increasing the dose, it is possible to find the minimum effective dose (on average 29.2 mg/d according to the study by Ray et al **[16]**) to limit oral intake to one litre per day for some patients, or even two to three litres per day to avoid the risk of overdose and hyponatremia **[17]**. As regards the safety of Minirin in cases of ID during pregnancy, a systematic review by Ray et al **[16]** of 53 pregnancies did not reveal any significant adverse effects in the mother or the newborn, or any increase in the incidence of prematurity.

The peripartum period is a high-risk period due to limited oral intake, whether the delivery is by caesarean section or vaginal delivery. In this context, Minirin can be introduced to support childbirth and analgesia or locoregional anaesthesia. Minirin may sometimes be indicated earlier in pregnancy for reasons of comfort when the polyuro-polydipsic syndrome is very severe: major fluid intake of up to 20 litres per day **[18]**, or severe hypernatremia **[19,20]**. When indicated, specific treatment with Minirin should be started in hospital to allow close clinical and biological monitoring. This monitoring should include fluid intake/output and daily weight measurement. Biological monitoring (blood ionogram) is also necessary to ensure that the treatment is well tolerated (hyponatremia in the event of Minirin overdose). A new biological check-up with measurement of urinary and plasma osmolality should be scheduled at a distance from the birth, and above all the disappearance of the polyuro-polydipsic syndrome should be ensured in order to confirm the diagnosis of gestational DI. This symptom may recur and should therefore be investigated in particular during subsequent pregnancies.

Conclusion

Gestational DI can occur in the absence of any obstetric pathology, in which case its pathophysiology can be explained by interactions between the placenta and ADH metabolism. Although there is no clear evidence of a direct link between gestational diabetes and pre-eclampsia, the frequent association observed between these two conditions may be explained by their occurrence in a high-risk environment. However, the polyuro-polydipsic syndrome is a symptom that is often trivialised by patients and may be reported spontaneously, so its frequent association with serious obstetric pathologies justifies its systematic investigation by questioning.

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