Gestational Diabetes Insipidus (GDI) Associated with Pre-Eclampsia

Abstract

Gestational diabetes insipidus (GDI) is a rare complication of pregnancy, usually developing in the third trimester and remitting spontaneously 4-6 weeks post-partum. It is mainly caused by excessive vasopressinase activity, an enzyme expressed by placental trophoblasts which metabolizes arginine vasopressin (AVP). The treatment requires desmopressin. A 38 year old G3P0A2 women with no significant medical history was admitted to obstetrical service on 36th week of gestation due to significant malaise, anorexia, nausea, vomiting, polyuria, nocturia, and polydipsia, worsening in the 2 weeks prior to presentation. Physical examination demonstrated decreased skin turgor, hyperactive tendon reflexes and no pedal edema, and her blood pressure was 170/100 mmHg, heart rate 67 beats/min and weight 60kg (BMI 23.1kg/m^2). Her laboratory results a month prior to admission showed normal basic metabolic panel and liver function tests. On admission she found to have urine osmolality112 mOsmol/kg (350-1000); serum osmolality 308mOsmol/kg (278-295); Urinalysis revealed specific gravity less than 1005 with proteinuria. serum sodium 151mmol/L (135-145); potassium 4.1mmol/L (3.5-5.0); Cl 128 mmol/L, urea 2.2mmol/L (2.5-6.7), creatinine 1.4 mg/dL, Bilirubin 1.3 mg/dL, AST 1270 U/L, alkaline phosphatase, 717 U/L, uric acid 10.1 mg/dL and INR 1.1. Full blood count was within the normal reference range. Patient underwent into emergent C-section a few hours after admission due to fetal distress. Post operatively patient remained polyuric and polydipsic. She was given DDAVP as needed for two weeks. A fetus was delivered at the 36th week without major problems. Two weeks post-partum the patient stopped the DDAVP. At 4 weeks post-partum, her sodium, serum and urine osmolality were within the normal reference range, and she no longer suffered from polyuria, polydipsia or nocturia. She remains clinically well.

Keywords: Nocturia; Polydipsia; Polyuria; Apgar; Eclampsia; Pre-eclampsia

Case Report

Volume 5 Issue 6 - 2017

Afsoon Razavi*, Muhammad Umair, Zehra Tekin and Issac Sachmechi

Department of medicine, Icahn School of Medicine at Mount Sinai/NYC Health+ Hospital/Queens, USA

***Corresponding author:** Afsoon Razavi, MD, Department of Medicine, Icahn School of Medicine at Mount Sinai/NYC Health + Hospital/Queens, Diabetes center, 4th floor, Suit P-432, Pavilion building, Queens hospital center, 82-68 164th street, Jamaica, New York, 11432, USA, Tel: +8183843165; Email: drafsoonrazavi@gmail.com

Received: July 25, 2017 | **Published:** August 16, 2017

Abbreviations: GDI: Gestational Diabetes Insipidus; AVP: Arginine Vasopressin; ADH: Antidiuretic Hormone; DDAVP: Deamino-8-D-arginin Vasopressin; NICU: Neonatal Intensive Care Unit; G3P0A2: Gravid3 Para0 Abortion2; HELLP syndrome: Hemolysis, elevated Liver enzymes, Low Platelets

Introduction

Gestational DI occurs only during pregnancy and the postpartum period. During pregnancy, women produce vasopressinase in the placenta, which breaks down antidiuretic hormone (ADH). GDI is thought to occur with excessive production and or impaired clearance of vasopressinase. Most cases of GDI can be treated with desmopressin, deamino- 8-D-arginine vasopressin (DDAVP), but not vasopressin. Diabetes insipidus is also associated with some serious diseases of pregnancy, including pre-eclampsia, HELLP syndrome and acute fatty liver of pregnancy. These cause DI by impairing hepatic clearance of circulating vasopressinase [1]. It is important to consider these diseases if a woman presents with diabetes insipidus in pregnancy, because their treatments require delivery of the baby before the disease will improve. Failure to treat these diseases promptly can lead to maternal or perinatal mortality.

Case Presentation

A 38 year old G3P0A2 women with no significant medical history and uneventful prenatal course was admitted to obstetrical service on 36th week of singleton gestation due to significant malaise, anorexia, nausea, vomiting, polyuria (around 9l/day), nocturia, and polydipsia, worsening in the 2 weeks prior to presentation. Her past medical history was unremarkable, she denied alcohol intake or smoking, and she was not taking any medication. There was no family history of endocrinopathy or liver disease. Physical examination demonstrated decreased skin turgor, hyperactive tendon reflexes and no pedal edema, and her blood pressure was 170/100 mmHg, heart rate 67 beats/min and weight 60kg (BMI 23.1kg/m^2). In view of elevated blood pressure she was suspected to have pre-eclampsia and given MgSO4. Her laboratory results a month prior to admission showed normal basic metabolic panel and liver function tests. On admission she found to have urine osmolality112 mOsmol/kg (350-1000); serum osmolality 308mOsmol/kg (278-295); Urinalysis revealed specific gravity less than 1005 with proteinuria. serum sodium 151mmol/L (135-145); potassium 4.1mmol/L (3.5-5.0); Cl 128 mmol/L, urea 2.2mmol/L (2.5-6.7), creatinine 1.4 mg/dL, Bilirubin 1.3 mg/dL, AST 1270 U/L, alkaline phosphatase, 717

U/L, uric acid 10.1 mg/dL and INR 1.1. Full blood count was within the normal reference range.

The 24-h urine output prior to desmopressin was 9000 ml/24. Considering the risk of dehydration in pregnancy, a water deprivation test was not performed. Patient underwent into emergent C-section a few hours after admission due to fetal distress. Post operatively patient remained polyuric and polydipsic. She was given DDAVP as needed for two weeks in different routes of administration with a significant response. More than 50% decrease in urine output was noted, as well as an increase in urine specific gravity. A male fetus with a 1-min Apgar score of 9 was delivered at the 36th week; he was transferred to NICU due to premature birth. Two weeks post-partum the patient stopped her DDAVP. At 4 weeks post-partum, her sodium, serum and urine osmolality were within the normal reference range, and she no longer suffered from polyuria, polydipsia or nocturia. She remains clinically well.

Discussion

Gestational DI is a rare complication of pregnancy occurring in two to four out of 100,000 pregnancies [2,3]. It usually develops at the end of second or third trimester of pregnancy and remits spontaneously 4-6 weeks after delivery [3,4]. Symptoms include hypotonic polyuria, polydipsia, fatigue, weight loss, decreased skin turgor and nausea, which usually develop over a few days, and may worsen in the subsequent days or weeks if this condition is not properly identified and treated [1,5]. Its pathophysiology is thought to result from increased degradation of arginine vasopressin (AVP) by a placental enzyme called vasopressinase. Vasopressinase is a cysteine aminopepdase of molecular weight 330 kDa, and is produced by the placental trophoblasts during pregnancy [6]. Throughout pregnancy, vasopressinase levels increase by 100,000 fold while placental mass grows, Serum concentrations can be detected as early as the 7^{th} week of gestation, reaching the maximum around the 40^{th} week, and are usually undetectable around the 6th week postpartum [7]. Being synthesized from the placenta, higher enzyme concentrations were observed in twin and triple pregnancies. After placental expulsion during delivery enzyme levels decrease rapidly, but remains elevated in the blood for couple of weeks postpartum.

There are substantial physiologic changes that occur during pregnancy to increase intravascular volume, including reduction of set point for serum osmolality for AVP hormone secretion and increased thirst in response to lower serum concentrations. In most of the pregnancies increased secretion of AVP by four fold maintains water balance despite increased degradation by vasopressinase, while pregnancy may unmask pre-existing Central or Nephrogenic Diabetes Insipidus, or lead to GDI which is more commonly seen in multiple gestations due to increased vasopressinase production from trophoblastic mass or with syndromes of hepatic dysfunction (e.g., HELLP syndrome, pre-eclampsia and eclampsia) due to impaired metabolism of vasopressinase by liver [8]. Affected individuals can be treated with DDAVP which is the vasopressinase resistant, synthetic form of AVP.

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